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GAS DISTENSION OF THE LATERAL VENTRICLES AT ENCEPHALOGRAPHY

G P PROBST

Dilatation of the fourth ventricle during the filling period of encephalography was assumed by OBERSON *et coll* (1969) from the enlargement of its height and was subsequently confirmed by others. This would also certainly mean greater volume though strictly speaking an increase in a single linear measurement is not necessarily the same as an increase in volume.

The present author has recently stated that convincing evidence exists that the third and the lateral ventricles may also become distended by gas during encephalography. This phenomenon would probably not be demonstrated in practice. The observation below will suggest however that this belief was incorrect as parts of the lateral ventricles are actually better suited for the demonstration of gas inflow distension than for example the fourth ventricle. Such parts are sizable occipital horns of tubular shape. Volume changes of these may be calculated with reasonable accuracy.

Observations. The figure depicts a tubular left occipital horn at moments a and b which means about three and fifteen minutes after the injection of the first partial volume of air. The films were taken in the sitting, ventrally tilted

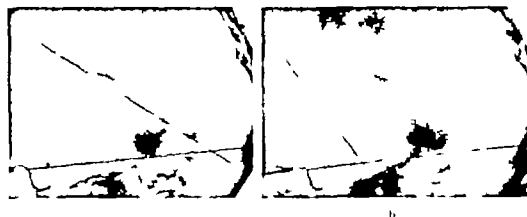


FIG. 1. (a) Ventriculogram of the lateral ventricle of a patient with a large occipital horn. (b) Ventriculogram of the same patient after injection of air. The size of the occipital horn and the adjacent bodies of the lateral ventricle are increased.

position. The unchanged focus-object distance is documented by the identical size of the skeletal structures on superposition of the film. The inclination of the patient's head was increased 20 degrees from the vertical between the moment a (apparent from the angle between the fluid level and theinion tuber-culum-sellae line). Additional air was injected between the moment a: a total of 20 ml cerebrospinal fluid was withdrawn and about double the amount of air injected. The size of the occipital horn as well as that of the adjacent bodies of the lateral ventricles had become obviously larger. The tubular shape of the horn with its blunt extremity and general retention of shapes makes it especially suitable for the calculation of its volume. The horn is considered to be a cylinder the diameters being taken as the means of the least and largest at the necks and the bulbous parts respectively. Both cylinders were regarded as being of equal length (30 mm) in order to exclude a possible source of error.

Film 1: length 30 mm $r=6$ mm. Film 2: length 30 mm $r=9$ mm. The cylinder volume at moment a is 3.4 ml and at moment b 7.6 mm: the difference being 4.2 ml or 124 per cent.

Discussion

Demonstration of the ventricular collapse phenomenon by the present author indicated that the contrary phenomenon also existed and raised the old problem of the true size of the cerebral ventricles. As the evidence for a distension effect was convincingly strong the task was first to prove it and secondly to establish

its extent. This single observation of the increase in volume of the posterior parts of the lateral ventricles during the first 15 minutes of a conventional encephalography may be regarded as significant and of importance in confirming the previously suggested existence of an artificial gas distension of the cerebral ventricles.

Nothing contradicts the conception that this phenomenon includes the lateral ventricles as a whole: consequently the a.p. films obtained later in the supine position may reveal distension of the anterior parts as well.

Because of the almost complete absence of distensibility of the cranial and spinal cavities a surplus of any gas volume introduced cannot be compensated for by an expansion of the system. Such compensation may be obtained by displacement of a corresponding volume of easily movable contents, i.e. intravascular fluid and presumably by an increased absorption rate of the CSF which is also believed to be involved in the mechanism that reestablishes the original pressure after a gas injection peak. This means a reduction in the brain volume as well as dilatation of the ventricular and subarachnoid compartments. Generally speaking the compression of the brain substance could be produced in three ways namely from inside outside or from both sides, which is finally a question of the distribution of the gas within the CSF spaces. As the gas can be directed predominantly to the ventricles or to the subarachnoid spaces the relative power of these effects is also dependent on the technical performance of the procedure and thus on the problem that is expected to become solved by the examination.

As filling of the ventricles is usually the first aim of any encephalography some degree of the gas distension phenomenon may be expected to be almost always produced though not as extensively as above. The subarachnoid spaces on the other hand may possibly become distended by the subsequent air filling whereby the brain substance may be subjected to additional compression from outside. The gas filled ventricles, however, cannot be compressed unless gas-losing manoeuvres resulting in a transfer of the gas from the ventricles to the subarachnoid spaces be performed: the collapse phenomenon will then be established.

The distension of the ventricles may be particularly striking if a surplus of air be injected as is the practice in our department where usually about twice as much air is introduced as cerebrospinal fluid withdrawn. This is in line with the recommendation by LINDGREN (1954) and seems to be a widely used manner of performing encephalographic examinations. The same effect may of course be expected if the air be introduced without withdrawal of fluid — also practised as a routine in some centres. Whatever the interrelations between the surplus of air and the size of the ventricles may be the suggestion that an equal fluid gas

exchange would be expected to reveal the ventricles in a more natural state than with a gas-excess exchange, seem, however, to be fairly reasonable.

The extent of the distension phenomenon seems also to be dependent on the technical performance of the procedure so that the latter should be as standardized as possible if the aim of the examination be the assessment of the ventricular size and if comparable examinations be intended.

The existence of the distension phenomenon at encephalography should be borne in mind in the assessment of ventricular size and the diagnosis of enlargement (atrophy or hypertrophy). Widened ventricles may suggest distended ventricles, a widened subarachnoid space in the young child may be a distension phenomenon rather than hypohydrat. Roundish superolateral aspects of the lateral ventricles should not automatically be regarded as sign of central atrophy. The septum-quadrate distance may also be expected to become considerably enlarged as occurred with the collapse phenomenon though in the opposite direction.

SUMMARY

The gas distension phenomenon of the cerebral ventricles is described and its relevance in the assessment of the size of the ventricles stressed.

ZUSAMMENFASSUNG

Das Gas-Ausdehnungs-Phänomen der zerebralen Ventrikel wird beschrieben und dessen Relevanz bei der Feststellung der Ventrikelgröße hervorgehoben.

RÉSUMÉ

Le phénomène d'extension par les gaz des ventricules cérébraux est décrit et l'auteur insiste sur son importance pour la mesure des dimensions des ventricules.

REFERENCES

- LINDORF, F. Handbuch der Neurochirurgie. Band II. Röntgenologie. Springer Verlag, Berlin-Göttingen-Heidelberg 1954.
- OSERSON, R., CANDAROFF, G. and RAAB, N. Height of fourth ventricle. Normal variation during pneumography. *Acta radiol. Diagnosis* 9 (1969) 193.
- PROBST, J. I. Rapid changes in the volume of the lateral ventricles at encephalography. *Acta radiol. Diagnosis* 12 (1972) 757.

ISOTOPI CISTERNOGRAPHY AND VENTRICULOGRAPHY IN FRONTOTHRMOIDAL ENCEPHALOMENINGOCELE

C SUWAKWELA V POSHYACHINDA and M POSHYACHINDA

The diagnosis of encephalomeningocele is usually made without difficulty when a cystic mass at the midline of the skull is associated with transmitted pulsation or pressure and with a definite intracranial communication. The diagnosis however may be difficult when the lesion lies hidden in the nose or when the mass is firm and solid: this has to be differentiated from a cyst or a tumour indigenous to the region. A false diagnosis of unciptal encephalomeningocele has led the present authors as well as others to negative intracranial exploration: on the other hand such growths presenting in the nose or pharynx have been thought to be nasal polyps and their removal by snare has been followed by meningitis or even death.

Demonstration of the cerebrospinal fluid spaces and the flow of cerebrospinal fluid with radioisotopes have proved valuable in the diagnosis of many neurosurgical conditions such as hydrocephalus and cerebrospinal fluid fistula (Brookshurst 1968; Di Cenzo et coll 1966, 1968). The present communication describes the application of this technique in 12 patients with encephalomeningocele in the anterior part of the skull.

The radiisotope outlined the extension of the subarachnoid space into the encephalomeningocele in all patients (Fig 2) the presentation being usually best in the scan at three hours after the injection although sometimes satisfactory at one hour. In one patient however the radiisotope in the herniation was only minimal at three hours but more definite at 24 hours.

Encephalography was also performed in the patients. Air entered the encephalomeningocele in only four patients; no leakage of air into the region of the neck nor the sac of the herniation occurred in spite of repeated manipulation in the remainder.

Extension of the ventricle into the herniation. Two patients had hydrocephalus in addition to a mass at the root of the nose. RISA was injected into one lateral ventricle through the coronal suture. The scan in one patient disclosed dilatation of the lateral ventricles with extension of the frontal horn into the sac of the encephalomeningocele (Fig 3). No extension of the lateral ventricle into the herniation was demonstrated in the other patient.

Cerebrospinal fluid scintigraphy also proved useful in demonstrating porencephalic cysts as well as investigating hydrocephalus.

Discussion

Attempts at the demonstration of the communication between the intracranial cavity and the cavity of the encephalomeningocele by means of dye and radiographic contrast media have met with limited success (ESILA et coll 1967 MOORE 1952 SIEVERS 1929 SUWAYWELA et coll 1966 1971). Air was evident in the herniation in only 7 out of 57 patients with fronto-ethmoidal encephalomeningocele.

LIN et coll (1968) described the entry of a radiisotope into areas in the subarachnoid space not demonstrated by air in patients with occipital hydrocephalus. The same was apparent with encephalomeningocele in the present material. Radiisotopic material appears to flow more readily into the herniation resulting in more positive results than at encephalography.

SUMMARY

Scintigraphy of the cerebrospinal fluid spaces is described in 12 patients with fronto-ethmoidal encephalomeningoceles. The procedures proved successful and informative in the demonstration of the intracranial communications of the mass.

ZUSAMMENFASSUNG

Scintigraphie der cerebrospinalen Flüssigkeitsräume wird bei 12 Patienten mit fronto-ethmoidalen Encephalomeningoceelen beschrieben. Das Verfahren erwies sich zum Nachweis der intrakraniellen Verbindungen der Masse erfolgreich und informativ.

RÉSUMÉ

Les auteurs décrivent la technique des ponctions et de la ligature pharyngale à 12 millimètres pour l'encephalocèle frontoethmoïdale. Cette technique est simple, sûre et efficace. Il y a eu une guérison évidente des malades d'encephalocèle frontoethmoïdale.

REFERENCES

- BARKER C. C. and FLOWERS J. A. Lacrimum allatum in the study of cerebral fluid flow. *J. Neurol. Neurosurg. Psychiat.* 31 (1968) 11.
- DICKER C. R. and MENDENHALL W. B. J. RISA cisternalography and RISA cisternalography. *Neuroradiology* 14 (1963) 18.
- and COOPER A. S. Jr. Evaluation of cisternal fluid dynamics by the ^{131}I isotope method. *J. Neurosurg.* 34 (1966) 741.
- ALBURN W. I. and BURR W. H. Technic of cisternal fluid flow in *A. J. Neurol. Clin.* 13 (1968) 218.
- LATA R. TORRES L. and VASQUEZ L. Unilateral, bilateral, hydrocephalic and bilateral atresia of the lacrimal passages. *Acta Ophthalmol. Kbh.* 45 (1967) 330.
- LESTER J. J., COOKSON R., FINE I. C. K., FLETCHER J. and VINCIGUERRA E. Radioisotope serum albumin RISA cisternography: the diagnosis of the ureal block in occulta hydrocephalus. *Radiology* 90 (1968) 36.
- MOORE P. M. Transnasal encephalomenigele. Laryngoscope, St. Louis, C. D. 69.
- STREIBER R. Über nasosorbitale Encephalocel mit besonderer Berücksichtigung eines durch Trepanation geheilten Falles. *Dtsch. Z. Chir.* 1929 (89).
- SUWANWEEA C. and HONGAPRABHAB C. Fronto-ethmoidal encephalomenigele. *J. Neurosurg.* (1966) 172.
- SILABOTY C. and SUWANWEEA N. Frontoethmoidal encephalomenigele. *Surgery, St. Louis* 62 (1971) 617.

ROENTGENOLOGIC DIAGNOSIS OF PANCREATIC ABSCESS

U TYLEN and H DENCKER

The diagnosis of pancreatic abscess is often difficult as evidenced by the fact that in about a third of the patients it is made only post mortem (ALTEMEIER & ALEXANDER 1963 DENCKER et coll 1972). The typical clinical course usually consists of an attack of acute pancreatitis followed a few weeks later by abdominal pain and high fever; a tender mass may be palpated in the epigastrium (ALTEMEIER & ALEXANDER, BOLOOGI et coll 1968 EVANS 1969). More often however signs of sepsis and toxæmia predominate (EVANS DENCKER et coll). Laboratory tests are usually of minor importance. Leucocytosis is common although wide variations may occur (STEEDMAN et coll 1967 EVANS). An elevated serum amylase is recorded in a quarter to a half of the patients (FARRINGER et coll 1967 EVANS).

Roentgenography may be helpful in arriving at the diagnosis. Gas bubbles in the retrogastric space will suggest a pancreatic abscess (FELSON 1951); an expansive lesion in the upper part of the abdomen combined with distension of a paralytic transverse colon, the colon cut off sign, may also be evident (BRASCHIO et coll 1962). A left pleural effusion (FARRINGER et coll STEEDMAN et coll)

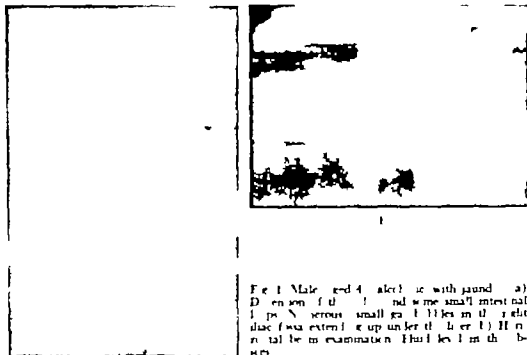


Fig. 1. Male aged 41, alcoholic with jaundice. (a) Demonstration of the duodenum and some small intestinal loops. Numerous small gas bubbles in the right duodenum extending up under the liver (l). It is not in the examination. Fluid levels in the bowel.

has been reported and displacement of the stomach or the duodenum may be revealed by a barium meal examination (ALTMAYER & ALEXANDER EVANS).

This investigation was carried out in an attempt to determine whether the diagnosis of pancreatic abscesses could be arrived at more rapidly by means of selective visceral angiography.

Material. A pancreatic abscess was diagnosed in 21 patients during the period 1951—1970. Different roentgenologic methods were used in 10 of these patients so that their value in establishing the diagnosis could be assessed. All the patients were operated upon and the findings verified. The size of the abscesses varied from approximately 5 to 20 cm in diameter.

Results

Roentgenography of the chest was always performed. Two of the 10 patients had a left pleural effusion and 3 had left or right basal atelectasis. The lungs of one patient were at first normal but at repeat examination basal atelectasis had developed.

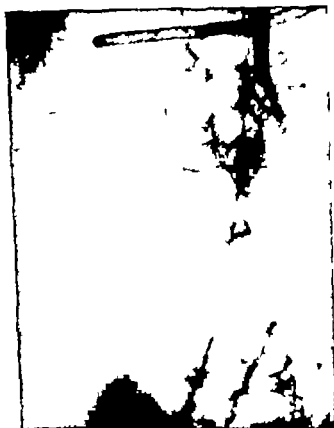


Fig 2 Same case as fig 1
Three weeks later. A
graph of the supero-
mesenteric artery. Mark 1
changes in arteries in
round head of pan.
Tortuous and irregular
parts of the superior
enteric, ileocolic and
colic arteries.

Roentgenography of the abdomen revealed changes in 4 of the
examined. Gas bubbles in an abscess were evident in the right iliac fossa
(2) and in the left flank (Fig 3) in 2 patients respectively. Expansion
in the upper part of the abdomen were present in another two patients.
Distension with a distended transverse colon in one and displacing the
the other patient.

Barium meal examinations demonstrated abnormalities in 8 out of
in 6 the stomach was displaced forwards by a retrogastric expansion
(4) and in the remaining 2 patients a minor deformation of the duodenum
was present.

Selective visceral angiography disclosed a pancreatic abscess in 6
examined. Displacement of the splenic, left gastric and intestinal arteries
depending on the localization of the abscess, occurred in 7 of these.



Fig. 3. Woman aged 45 with diverticulum of the colon and high temperature two weeks before the pancreatic abscess. Left-sided pleural effusion. (a) One month after the first attack of pancreatitis small foci were evident in the left flank. Probable abscess from ectopic diverticulum. Arteriography two weeks later. Slight regular stenosis of the splenic stem. Increased middle colic artery tortuosity, irregular and displaced medially indicating pancreatic abscess.

3-4). The degree of displacement was often marked and corresponded with the size of the abscess at operation. No arterial displacement was evident in 3 patients, in one of whom the abscess was extremely small (Fig. 5) while though very large in the other patient extended mainly in the retroperitoneal space (Figs 1-2). Smooth and usually rather small stenotic arterial changes were noted in 8 patients, the splenic artery being mostly affected (Fig. 3). Increased tortuosity and a slightly irregular lumen of the pancreatic arteries were demonstrated in all the patients and similar changes in the intestinal arteries, mainly the middle colic artery, were present in 6 patients (Figs 2, 3). Arterial occlusion was not recorded. Venous lesions consisting of compression or occlusion of the splenic or superior mesenteric veins with collateral circulation were evident in 7 patients (Fig. 5).



Fig. 4. Man aged 55 with pancreatitis two months previously developed severe abdominal pain. a) Barium meal examination. Anterior displacement of the stomach. b) Angiography. Displacement and stretching of the left gastric artery. The first part of the splenic artery irregular and pancreatic arteries both irregular and tortuous.

Discussion

The prognosis in pancreatic abscess depends above all on early diagnosis and operation (BREWER 1907, ALTMENZER & ALEXANDER, DENCKER et coll.). The cause of the high mortality rate, close to 50 per cent, is the difficulty in recognizing the early clinical signs, laboratory tests being of little aid (STEEDMAN et coll., EVANS, DENCKER et coll.).

The roentgenologic examinations contributed to the diagnosis of the condition in all patients. Roentgen examination of the chest, however, revealed only pleural effusion and basal atelectasis, findings that were quite unspecific and present in only half the patients. The low frequency of positive signs may, at least partly, be explained by the fact that the patients with this disease are usually in a poor condition and unfit for a thorough examination.

The demonstration of changes in conventional films of the abdomen occurs to the same extent as in those of the chest. Gas bubbles in the retrogastric space are said to be pathognomonic (FELSON 1957), but an abscess may extend far from

common the diagnosis is often possible. Other causes of gastric displacement such as tumours of the stomach or retroperitoneal tissue, cannot however be excluded.

The roentgenologic diagnosis with the exception of the finding of gas bubbles in the abscess has thus been based on indirect signs. Selective visceral angiography however directly indicates the abscess and its origin by demonstrating vascular changes in the pancreas and the surrounding organs. Moreover the size of the abscess may be estimated by the degree of vascular displacement. The abscess in this material were usually large so that the marked displacement of the vessels made the diagnosis easy. In one of the patients however an abscess, less than 5 cm in diameter at operation, compressed the veins. This was important as the barium meal examination indicated that the abscess caused only slight deformation of the duodenum. It was diagnosed early only by angiography (Fig. 5).

A pancreatic abscess and a pseudocyst cannot be differentiated by angiography since both cause similar vascular changes. Differentiation may however usually be based upon clinical data when the pancreatic origin of the disease becomes evident. It may be stated that as a rule the arterial alterations are perhaps more marked in pancreatic abscess. The differentiation between pancreatitis without abscess or pseudocyst and pancreatitis with abscess or pseudocyst depends primarily on the absence of marked vascular displacement in the former. Exceptions to this rule may however occur as in two patients in this material.

The investigation suggests that the possibility of a pancreatic abscess is an indication for selective visceral angiography since it enables an early diagnosis of even fairly small abscesses.

Acknowledgement

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SUMMARY

The roentgenologic contribution to the diagnosis of pancreatic abscess in 10 patients is discussed. Selective visceral angiography was performed in 9 of the patients. It appeared to be the most reliable method and is particularly recommended.

ZUSAMMENFASSUNG

Der roentgenologische Beitrag an die Diagnose eines Pankreasabszesses bei 10 Patienten wird besprochen. Selektive viszerale Angiographie wurde bei 9 der Patienten vorgenommen. Diese scheint die zuverlässigste Methode zu sein und wird besonders empfohlen.

RÉSUMÉ

Les auteurs examinent la contribution de la radiologie au diagnostic d'abcès pancréatique chez 10 malades. Un anamnésis, l'exercice lective a été fait chez 9 de ces malades. 11) par cette méthode la plus fidèle et est particulièrement recommandée.

REFERENCES

- ALTMUTH W. A. and ALVARADO J. W.: Pancreatic lesions. Arch Surg, 87, 1967, 80.
 BERLIN J. I., SPITZ H. B. and ELIASO B.: The abdominal fat necrosis sign. Radiology, 100, 1971, 567.
 BOLOGNI H. J. and CHURCH M. I.: Pancreatic lesions and lesser omentum laceration. Surg Gynec Obstet 16, 1968, 1301.
 BRASCHIO D. J., REYNOLDS I. N. and ZAKS L.: The radio opaque colon-cut-off sign in acute pancreatitis. Radiology 77, 1961, 63.
 BRINTON C. F.: The technique of draining recurrent abscesses of the pancreas. Surg Gynec Obstet 5, 1907, 344.
 DICKER H., LINDNER C. and FRIEDL S.: Surgical aspects on pancreatic lesions. Acta medicand 138, 1952, 609.
 ELLIS C.: Pancreatic abscess. Amer J Surg 11, 1961, 53.
 FARRIS R. J., L. ROBBINS L. B. and L. GALT D. R.: Abscess of the pancreas. Amer Surg, 33, 1969, 131.
 FELSON B.: Gross lesions of pancreas. J Amer med Ass 163, 1957, 637.
 STEEDMAN R. A., DODRINE R. and CARTE R.: Surgical aspects of pancreatic lesions. Surg Gynec Obstet 125, 1967, 77.
 STEIN C. N., KALSER M. H., SARIAN N. N. and ENARLITIS A. I.: An evaluation of the roentgen changes in acute pancreatitis: correlations with clinical findings. Gastroenterology 36, 1959, 354.

WIDTH OF THE PAROTID MAIN DUCT IN HEALTHY SUBJECTS

A sialographic investigation

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The abnormal roentgen appearances of the parotid gland have received considerable attention (RAUCH 1959 GARGSI 1963 PREIFFER 1968 SCHULZ 1969). Both local and general diseases may produce morphologic changes in the gland tissue that can be differentiated radiologically. Inflammatory changes (adenitis) present essentially two distinct sialographic appearances: one of punctiform *microcalcifications* peripherally in the salivary ducts unaccompanied by changes in the parotid main duct (ductus Stenon) and the other of dilatation of this duct as the most prominent feature. The latter variant is considered to indicate infection arising from the mouth as in parotitis resulting from dehydration or as a result of obstruction of the duct; the other variant is characteristic of sialoadenitis with an autoimmune background as in Sjögren's syndrome or rheumatoid arthritis (PAYNE 1940 RUBIN & HOLT 1957 LENOCH et coll 1964 BLATT 1964 SEIFERT 1965 PATEY 1965 1969 BEVENDO-KAPLUSCINSKA & ZOLICZYNSKI 1967 ERICSON 1968 LAUDENBACH et coll 1969).

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Table 1. Salivary gland measurements of 184 healthy subjects. The values are the mean of the measurements of the main duct and the accessory ducts.



These basic radiographic appearances of sialoadenitis are however increased by those in which the origin of the primary condition may be obscure. The diagnosis is furthermore complicated by the fact that the lumen of the parotid main duct may vary considerably (OPPENHEIM & WING 1960, HETTWER & TOLSON 1968) furthermore its normal limits have not been satisfactorily established. It was therefore considered of interest to examine more closely the radiographic appearances of the parotid main duct in apparently healthy subjects and trying to assess the factors that normally bear on the width of the duct.

Material. This consisted of 92 healthy subjects chosen at random and made up of 31 women aged from 26 to 64 (mean 49.8 years) and 61 men of the same age range and a mean of 48.8 years. They were examined with special reference to their general condition and the salivary gland (FRICSON 1968). No evidence of salivary gland disorders was recorded nor was any suggestion of past or present diseases that might have affected the gland. The lateral projections of all 184 parotid glands were examined. The material was identical with that used in earlier investigations (FRICSON 1968, 1969, 1970, 1971) to which the reader is referred for details.

Method. The radiographic examination of the parotid gland was carried out with lateral and a.p. projections by a method that has been reported elsewhere (FRICSON 1968, 1970). The central ray was directed through the middle of the gland for the lateral projection at 78° to the sagittal plane and for the a.p. projection perpendicular to the film plane and parallel to the ascending ramus of the mandible. FFD 10 cm. The contrast medium Urografin 60 was injected in fractionated doses by a standardized technique. The enlargement factor was approximately 1:1.1. Five exposures were made in the lateral projection for each gland: one before the injection, three during the injection at different degrees of filling, and one five minutes after the injection was com-



Fig. 2. Sialograms of the left parotid glands from two healthy subjects with glands of equal size. The width of the main duct and the ramifications differ in width. The salivary flow rates were within the normal range.

pleted so that the excretion could be examined. The amount of contrast medium injected during the filling phase was 0.6 to 1.2 ml.

The width of the ductus Stenon in the lateral projection was recorded. The measurements were performed directly in the third sialogram exposed during the injection phase at maximum filling with a magnifying glass graduated in tenths of a millimetre. They were made along the whole of the excretory duct and the maximum width was noted. No measurements were performed nearer a branch than a millimetre. The lateral sialograms were also used as a basis for estimating the size of the parotid gland so as to be able to ascertain whether any relationship between it and the lumen of the duct existed. Earlier investigations have revealed an extremely close correlation between the area of the lateral projection and the total volume of the parotid gland, with $r=0.95$ (ERICSON & HEDRÉ 1970). Since the area is almost directly proportional to the volume, it may be used to indicate the size of the gland.

The rate of secretion of both parotid glands was recorded at rest and after oral stimulation with one and ten per cent citric acid to determine any relationship between the secretory capacity of the parotid gland and the width of the lumen of the duct. The reader is referred to the author's earlier reports for a detailed account of the method and the secretion values (ERICSON 1968, 1969, 1971).

Results

The parotid main duct emerged into the salivary papilla in the oral vestibulum in all 184 glands. The width of the lumen of the duct varied within the gland and between glands of different subjects. The duct was usually straight,



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Fig. 3. S. 1.6 mm of the left (not enlarged) from a healthy subject (the section is stained with hematoxylin). A. 1.6 mm of the main duct of the pancreas. The width of the lumen of the main duct with the widest part.

but sweeping convolutions were also noted in the absence of both obstruction and dilatation. The maximum duct width was always measured in the gland and the lumen diminished in the distal and proximal direction (Figs 1 to 3). The maximum width of the ductus Stenosi on the right and left sides is given in Table 1 for men and women and for large and small glands.

The maximum lumen width ranged from 0.1 to 1.0 mm with a mean of 0.20 mm. There was no right — left difference and the correlation coefficient r was 0.87. The values are approximately normally distributed. The standard deviation of the mean was 0.6; according to the 2 σ rule this gives a 95 per cent confidence interval for healthy glands ranging from 0.8 to 3.2 mm. Only 7 (or 3.6 per cent) of the glands fell outside these limits.

Differences in the lumen of the duct that could be ascribed to sex and gland size were observed (Table 1). The lumen was significantly wider in the men than in the women and in the larger than the smaller glands; the differences were fairly low, however, with means of 0.3 and 0.4 mm respectively.

The maximum intra subject width of the lumen on the right and left sides was compared. From the means of these (Table 1) and from the correlation coefficient of 0.87 for the left — right ratio it is evident that the lumen in healthy glands has about the same width on the two sides. The absolute value of the difference in width between the two sides was calculated to determine the greatest right — left probability. The mean difference between the right and left sides was 0.19 mm with a standard deviation of 0.24 (Table 2). The greatest difference between the sides, disregarding the pair with multiple strictures, was 0.9 mm. By applying the 2 σ rule to all 92 pairs a 95 per cent con-

Table 1

Maximum width (mm) of the projection of the parotid main duct in lateral sialograms of 184 parotid glands from 99 subjects. Means (\bar{x}) standard error (SE) standard deviation (SD) and t

	Range	$\bar{x} \pm SE$	SD	t significance
Right parotid gland	0.9-4.0	2.0 ± 0.06	0.6	Not signif
Left parotid gland	1.0-3	2.0 ± 0.06	0.6	
Right + left parotid glands	1.0-4.0	2.0 ± 0.06	0.6	
Men	1.0-4.0	2.2 ± 0.07	0.6	$t = 3.0$
Women	0.9-3	1.9 ± 0.05	0.6	
Lateral area of parotid				
Less than "	0.9-3.2	1.8 ± 0.05	0.5	$t = 4.31$
Greater than "	1.3-4.0	2.0 ± 0.06	0.6	

significant $p < 0.01$

highly significant $p < 0.001$

Table 2

Mean right-left difference (absolute value) and standard deviation of the mean SD and the range of the right-left difference for maximum width (mm) of the main duct as projected in the lateral sialogram

	\bar{x}	d	SD	Range
Right-left difference in maximum width of main duct	99	0.19	0.24	0-1.3

Table 3

Correlation coefficients for combining the maximum width of the parotid main duct in 184 glands and number of venous

	Sex	Age	Size of parotid	Rate of secretion			
				1	6	10	Rest
Maximum width of the parotid main duct	-0.92	0.18	0.33	0.20*	0.23	0.30*	0.10

Table 4

Regression coefficient, their SE and level of significance on step 14 regression model of maximum width of the lumen of the parotid main duct of 184 parotid glands in 9 subjects

Regression	Regression coefficient	Multiple R	Partial correlation coefficient
Intercept	0.017 0.019	0.33	0.33
Sex	0.916 0.07	0.37	-0.19
Rate of secretion stimulated with 10 min of stimulation	0.007 0.007	0.39	0.10
Age	0.006 0.00	0.41	0.01

fidence interval of 0.7 mm for the maximum intra subject right — left difference at the same degree of filling is obtained. A total of 96 per cent of the subjects of this material lay within this interval. The discrepancy in width between the two sides for 87 per cent of the pairs was less than the mean difference plus one standard deviation (total < 0.7 mm). This bears out the impression that in the healthy subject close agreement between the width of the parotid duct on the right and left sides normally exists.

The correlation coefficients were calculated to determine whether the width of the duct lumen was related to sex, age, gland size or rate of secretion. A significant or almost significant correlation with the maximum width of the duct was evident for all these factors although the coefficients were low (Table 2). The stimulated but not the unstimulated secretion was significantly correlated with the duct width. The correlation coefficients increased with the degree of stimulation — that is to say the lumen width increased to some extent with the maximum secretory capacity.

Because the sex, age and rate of secretion are all correlated with the size of the parotid gland (FRICSON 1970, 1971) the correlations between these variables and the width of the duct presented in Table 3 might conceivably be fictive and actually a manifestation of gland size (see FRICSON 1968). The relationship between the duct lumen and the variables was examined by multiple regression analysis to determine whether the gland size is in fact reflected in the correlations of these variables. The regression coefficients were calculated with respect to each other factor included in the analysis. When the size of the gland is considered only the sex variable was significantly correlated with the duct lumen while the age and secretion variables were without significance (Table 4). The multiple correlation coefficient R was 0.41.

Discussion

The investigation was performed in healthy subjects with neither current nor previous symptoms from the salivary glands nor was there any history of any disease likely to involve the glands.

The measurement points could not be defined anatomically so that an attempt was made to find the greatest width of the duct lumen. This procedure may appear to be a shortcoming because it would presumably be difficult sometimes to determine the points on the duct lumen that would reliably delimit the maximum width. In addition such width of the parotid duct may theoretically be influenced by variations in the degree of filling. These factors presented no problems however with the standardized technique used. They could obviously be overcome by the high correlation coefficient of 0.81 between the maximum width of the duct lumen on the two sides and by the mean widths of the two lumina being identical and the mean left — right difference small (Table 2). The error of the method was thus of little if any significance to the results. Because the radiologic part is reproducible (ERICSON 1968) and the measurement procedure simple the means and the 95 per cent confidence interval may be used as a reference, and applied routinely in clinical work.

The inter subject variation in duct lumen width was large but the right — left difference for the individual subject on the other hand was small. A difference exceeding 0.7 mm may thus be regarded as abnormal with a 95 per cent probability. A close agreement between the size of the right and left parotid glands in adults has been given in an earlier investigation (ERICSON 1970). WIEDEMANN (1931) reported symmetric development of the two glands in children. The statement by THOMAS (1941) and GARUSTI (1964) that the structures of the two glands vary considerably even in the same subject is thus not confirmed.

The inter subject variation in the maximum width of the parotid duct lay between the limits of 0.8 and 3.2 mm with a 95 per cent probability. A maximum of 4 mm was measured in some instances. The values are higher than could be considered normal in previous investigations (OPPENHEIM & WING 1960; HETTWER & FOLSON 1968; PFIZFER 1968). The largest lumina all occurred centrally in the gland contradicting the report of PFIZFER (1968).

It is evident from the results that women have slightly narrower duct lumina than men in glands of comparable size and that no correlation between the width and age or secretory capacity exists. HETZAR (1942) and GARUSTI (1964) stated that the duct was narrower and that there was greater polymorphism in women than men and WIEDEMANN (1931) observed the same sex difference in children none of these workers gave measurements. The differences are, however too small to be of practical significance. The observation by HETTWER & FOLSON (1968) that the lumen of the duct increases in width with age was

not verified. No investigations of comparable size and carried out with an analytic procedure have been previously reported.

The regression analysis revealed that the strongest correlation with the maximum width of the lumen was obtained with gland size, although the correlation was remarkably weak and accounted for only a small part of the inter-subject variance in the width. Other factors not covered by the analysis must therefore together be of greater significance in the individual variation in the width of the ductus Stenoni; these will probably include genetic variables. In this respect, however, the effect on the variation in duct width of local factors cannot be disregarded — a factor that was not observed by the subjects themselves or that produced symptoms so remote as to be ignored. The agreement between the values for the left and right glands suggest, however, that local factors fail to exert a major influence on the width of the duct.

SUMMARY

The main duct in sialograms of 181 parotid glands was examined in 91 healthy subjects. The maximum width of the lumen of the duct measured and the means and standard deviations were calculated. Gland size and sex proved to be correlated to duct width though the coefficients were low. No correlation was evident between age and secretory capacity.

ZUSAMMENFASSUNG

Der Hauptgang von 181 Speicheldrüsen wurde bei 91 gesunden Personen in Sialogrammen untersucht. Die maximale Weite des Lumens des Ductus wurde gemessen und Durchschnittswert und Standardabweichungen berechnet. Die Größe der Drüse und das Geschlecht waren zur Weite des Ductus korreliert, obwohl deren Korrelationskoeffizienten niedrig waren. Keine Korrelation fand sich zwischen dem Alter und der sekretorischen Kapazität.

RÉSUMÉ

Le canal principal de 181 glandes parotides chez 91 sujets en bonne santé a été examinée par sialographie. L'auteur mesure la largeur maximale de la lumière du canal et a calculé les moyennes et les déviations standards. La taille de la glande et le sexe sont en corrélation avec la largeur du canal bien que les coefficients de corrélation soient petits. Il n'y a pas de corrélation évidente entre l'âge et la capacité sécrétoire.

REFERENCES

- BILANDO KAPURCINSKA B and ZIEGLERMAIER S L: Sialography in inflammatory lesions of the salivary gland. *Int Rev Radiol nucl Med* 31 (1967) 798.
BLATT I M: Otitis externa and benign lymphoepitheliomatous (The pyogenic parotitis-Göteborg-Sjögren syndrome-Mikulicz disease complex). *Otolaryngoscope* 74 (1964) 1684.

- ERIKSON S. The parotid gland in subjects with and without rheumatoid arthritis. A sialographic and physiologic study. *Acta radiol Suppl* No 275 (1968)
- An investigation of human parotid saliv. secretion rate in response to different types of stimulation. *Arch oral Biol* 14 (1969) 591
 - The normal variation of the parotid size. *Acta otolaryng* 70 (1970) 294
 - The variability of the human parotid flow rate on stimulation with citric acid with special reference to taste. *Arch oral Biol* 16 (1971) 9
 - Size of the normal parotid gland. *Acta radiol Diagnosis* 1 (1972) 69
 - and HEDON M. A clinical roentgenologic method of calculating the volume of the parotid gland. *Oral Surg* 29 (1970) 536
- GARLES G. F. Swellings of the parotid region. Sialography as an aid in differential diagnosis. *Radiology* 3 (1963) 364
- The salivary glands in radiological diagnosis. *Bibl radiol Fasc* 4 S. Karger Basel 1964
- HETTYER K. J. and FOLSON T. C. The normal sialogram. *Oral Surg* 26 (1968) 790
- HETTER W. *Die Sialographie*. Georg Thieme Verlag Leipzig 1942
- LA DENBACH P., BOURNEAU M., MOREAU R. et BORDHURAEF C. Essai d'étiologie sialographique. *Rev Stomat* (Paris) 70 (1969) 19
- JENNICH FR., BARMON A., JANKOVA D. et coll. The relation of Sjogren's syndrome to rheumatoid arthritis. *Acta heum scand* 10 (1964) 297
- ORLANDER H. and WREN M. Sialography and surface anatomy of the parotid duct. *Arch Otolaryng* 71 (1960) 80
- PATRY D. H. Inflammation of the salivary glands with particular reference to chronic and recurrent parotitis. *Ann roy Coll surg Engl* 36 (1965) 26
- Diagnosing parotid calculi. *Brit med J* 4 (1969) 687
- PAYNE R. T. Pneumococcal parotitis. *Brit med J* 1 (1940) 267
- PRETZNER K. *Die Röntgendiagnostik der Speicheldrüsen und ihrer Ausführungsgänge*. / *Handbuch der medizinischen Radiologie* Band 8 S. 300 Springer Verlag Berlin 1968
- RALPH S. *Die Speicheldrüsen des Menschen*. Georg Thieme Verlag Stuttgart 1959
- RUBIN PM. and HOLT J. F. Secretory sialography in diseases of the major salivary glands. *Amer J Roentgenol* 77 (1957) 575
- SCHULZ H. G. *Das Röntgenbild der Kopf- und Halsspeicheldrüsen*. Johann Ambrosius Barth Leipzig 1969
- SEITZ G. *Die pathologische Anatomie der Speicheldrüsenerkrankungen (Sialadenitis Sialadenose Sialome Syndrome)*. Hals Nas u Ohrenheilk 1 Teil 13 (1965) 1
- THOMA K. H. The use of radiopaque diagnostic media in roentgen diagnosis of oral surgical conditions. *Amer J Orthodont* 27 (1941) 64
- WITZMAN H. R. Sialography in childhood. *Z. Kinderheilk* 69 (1961) 133

TIP OF THE LIVER IN INTUSSUSCEPTION OF THE BOWEL IN INFANCY AND CHILDHOOD

HAKAN JORULF

The roentgenographic diagnosis of an intraperitoneal effusion usually consists of the demonstration of fluid between the lateral boundaries of the peritoneal cavity and the gas-distended intestines (LAURFELL 1973, 1976, 1977; IRIMANN, DALL 1960, 1968). An additional sign is that the tip of the liver, e.g. the lateral inferior margin of the right hepatic lobe is marked (LAURFELL 1973; BUDIN & JACOBSON 1967; MAROLLES & STONNE 1967). Even small amounts of fluid should be recognized (JORULF to be published). However, intussusception of the large bowel may distort the criteria usually applied for the detection of intraperitoneal fluid, a fact that appears not to have been considered previously. This communication presents a retrospective analysis of the appearances of the tip of the liver in conventional films of the abdomen in a series of 276 cases of intussusception of the bowel and the problems involved in recognition of intraperitoneal fluid.

Material. A total of 300 patients with intussusception were subjected during the period 1952–1970 on admission to contrast examinations of the large bowel. The records of 276 of the cases included a complete series of conventional



Fig. 1 a) Right flank. Tip of liver marked by contiguous intussusception. b) hepatic flexure.
 b) Barium enema examination.

roentgenograms which form the basis of the present review. The diagnoses were confirmed by barium enema examinations or laparotomy. The youngest patient was 15 days and the oldest 12 years of age.

Technique of roentgen examination and results. The films of the abdomen invariably included the flanks. The examinations were performed with the patients supine and with vertical rays as well as in the left lateral decubitus position with horizontal rays. The tip of the liver, the spleen and any signs of intraperitoneal fluid were recorded. The findings were related to the localization of the apex of the intussusception as demonstrated by barium enema and exceptionally in survey films of the abdomen.

The tip of the liver was demonstrated in 180 patients but not in the remaining 96 patients (Table 1). In 81 of the latter the liver margin could not be identified and was continuous with the adjacent area of the abdomen. Small amounts of gas and mottled faecal matter in the remaining 15 patients indicated

Table 1

Table of the liver as demonstrated in conventional films of the abdomen related to the fat-intussusception

Site of fat-intussusception		No. of patients with fat-intussusception	No. of patients with fat-intussusception demonstrated	per cent	per cent
Oral to hepatic flexure ileum	Cecum	5	1 (4)		
	Ascending	5	1 (3)		
		115		8	18
		37		30	81
Aboral to hepatic flexure	Transverse (right)	43	11 (3)		
	middle	40	10 (1)		
	left	3	3 (1)		
	Descending	6	(3)		
	Rectosigmoid	1	1 (1)		
Total		144		38	31
		6		9	3

No. of patients with gas and fecal material adjacent to the lip of the bracket

the presence of bowel loops adjacent to the liver. With intussusception in the hepatic flexure the right flank had a homogeneous appearance (Fig. 1) in 81 per cent of patients while this was less frequent when the intussusception was situated above or below this region i.e. in 18 and 31 per cent of patients respectively (Table 1). An inconspicuous stripe of fat indicated the position of the tip of the liver in two patients with the apex of the intussusception in the ascending colon as well as in 4 with the apex at the right hepatic flexure (Fig. 2). A mobile caecum was demonstrated by the barium enema examination in 20 patients (7 per cent).

Intraperitoneal fluid was evident in 6 instances, interposed between gas-distended intestines and either flank or between intestinal coils. The tip of the liver was not demonstrated and all 6 patients had obstructive ileus.

The amount of intraperitoneal fluid should be increased in complicating ileus with resultant blurring of the hepatic margin. This partially explains the fact that the incidence of obstructive ileus with a visible liver tip was only 15 per cent (Table 2) while when the tip was not identifiable it rose to 35 per cent. Fluid in the intestines is another factor that may contribute to the blurring in the latter group. However with the intussusception at the hepatic flexure and no hepatic margin demonstrable the incidence of obstructive ileus was

Tabl 2

Incidence of obstructive ileus related to demonstrated tip of the liver

	No. of cases	Obstructive ileus
Tip visible	180	27 (15 %)
Tip not visible	96	34 (35 %)
Total	276	61 (22 %)

Tabl 3

Incidence of obstructive ileus in undemonstrable liver tip related to site of intussusception

Site of intussusception	No. of cases	Obstructive ileus
Oral to hepatic flexure	28	9 (32 %)
Hepatic flexure	30	8 (27 %)
Aboral to hepatic flexure	38	19 (50 %)
Total	96	34 (35 %)

only 20 per cent (Table 3) compared to 35 per cent in the whole material obviously the probability of intraperitoneal fluid hiding the tip in this group is negligible

The incidence of obstructive ileus rose to 50 per cent with no demonstrable tip of the liver but with the intussusception located aboral to the hepatic flexure. Since it is reasonable to assume that intraperitoneal fluid should be the single factor to account for the blurring of the tip of the liver in the additional patients with obstructive ileus above the mean in the whole series (35 per cent) fluid should have been present in 6 patients of this group. However clear evidence of fluid in 2 patients only indicates the difficulty in recognizing fluid roentgenologically particularly with complicating obstructive ileus.

The lower pole of the spleen was demonstrated in the conventional films of the abdomen only in 28 per cent of patients the rate being 41 per cent in the group with the intussusception proximal to the hepatic flexure as compared to 11 per cent when it was situated distally. Intraperitoneal fluid invariably prevented the demonstration of the lower pole of the spleen.



Fig. 2



Fig. 3

Fig. 2 Right sided Intussusception with peritoneal hepatic flexure. Only small triangle of tissue adjacent to tip of liver indicates the margin.

Fig. 3 Intussusception of transverse ileum with displacement of hepatic flexure medially. Tip of liver well demonstrated but is been not visible.

Discussion

The roentgenologic approach to reduction of an intussusception of the large bowel by barium enema has for long been controversial. However GIFFLI et coll (1972) have suggested that this method of treatment is safe and effective. The only contraindication is complicating obstructive ileus with peritonitis and associated intraperitoneal fluid, signs that should suggest intestinal gangrene. The sources of error inherent in roentgenologic assessment of intraperitoneal fluid in intussusception of the bowel must consequently be thoroughly appreciated and recognized. Data derived from the present series suggest that a false positive diagnosis of intraperitoneal fluid may be made unduly exaggerating the risk of a diagnostic barium enema examination and reduction of the intussusception. Two factors may account for this error. First, intestinal loops devoid of gas and faecal matter interposed between the hepatic flexure and the peritoneum adjacent to the liver tip may simulate intraperitoneal fluid. Secondly the roentgen ray absorption of an intussusception containing prolapsed intestine and mesentery will be almost equal to that of the liver with consequent obliteration of its edge. Only rarely are small amounts of gas or faecal matter retained in the portion of the bowel involved to help in this differentiation. With the

intussusceptum propagating in the ascending colon the space ordinarily present between the large bowel and the tip of the liver will gradually narrow. The orientation of the hepatic flexure is from behind forwards and cranially which means that a fairly large part of an intussusceptum may be contiguous to the lower border of the liver. This may account for the effacement of the liver margin simulating the presence of intraperitoneal fluid. On the other hand with the intussusception advancing aborally the hepatic flexure may be displaced towards the midline of the abdomen (SCHATZKI 1939 FRIMAN DAIL 1960) and facilitate the accumulation of fluid or the interposition of the small intestine between the hepatic flexure of the colon and the lateral bounds of the peritoneal cavity adjacent to the liver tip (Fig. 3). Similarly a mobile caecum by predisposing to interposition of small intestinal loops lateral to the colon may interfere with the recognition of fluid in the right flank. It is most important to determine whether the inability to define the tip of the liver on conventional roentgenography of the abdomen be due exclusively to intraperitoneal fluid or to other factors as well. Such fluid recognized by the application of the usual criteria was demonstrable only in those patients with complicating obstructive ileus and necessitated the bowel loops being distended by gas. The frequent failure to demonstrate the tip of the liver in the presence of the complication mentioned may have been due to the intussusception being located in the contiguous part of the bowel, interposition of the small intestine possibly containing fluid or fluid accumulated underneath the liver or a combination of these factors. This differential diagnostic problem may be solved by a repeat examination of the flanks of the abdomen with the patient in the lateral recumbent position (LAURELL 1927 a, FRIMAN DAIL 1960 JOURNAL to be published). This procedure was not tried in the present series.

Examination of the right flank with 10 to 15° lateral inclination of the central ray should aid in the demonstration of the hepatic tip in intussusception of the hepatic flexure of the colon. Conversely inability to identify the tip with this technique suggests intraperitoneal fluid. However should the bowel harbouring the intussusceptum in the right flank be devoid of gas no safe conclusion can be drawn. If peritonitis be present or considered likely a diagnostic barium enema will however facilitate recognition of intraperitoneal fluid, particularly from inspection of the flanks.

SUMMARY

The roentgenographic diagnosis of intraperitoneal fluid with special reference to the appearance of the hepatic margin as reviewed in a series of 276 consecutive cases of intussusception of the large bowel in infancy and childhood. Errors in interpretation resulting in false positive diagnosis of fluid predominated when the intussusception was situated at the hepatic flexure. The differential diagnosis is considered.

ZUSAMMENFASSUNG

Die roentgenologische Diagnose intraperitonealer Flüssigkeit unter besonderer Berücksichtigung des Bildes der Leberbegrenzung wurde an einer Serie von 26 aufeinander folgenden Fällen von Intussuscat in der Duodenum bei Säuglingen und Kindern zum erstenmal beschriebenen Fehler der Interpretation, die zu einer falschen positiven Diagnose auf Intussuscat führten, unterworfen. Eine Invagination in der Gegend der Flexura hepatica gelegen war. Die Differentialdiagnose wird besprochen.

RÉSUMÉ

L'auteur recueille l'erreur diagnostique radiologique de la présence de liquide dans le péritoine particulièrement en ce qui concerne l'image du bord hépatique dans une série de 26 cas consécutifs d'invagination de gros intestin chez l'enfant et l'enfant. Les erreurs d'interprétation aboutissent à un faux diagnostic positif d'épanchement intraperitoneal prédominant quand l'invagination est située à l'angle hépatique du colon. L'auteur étudie le diagnostic différentiel.

REFERENCES

- BUDIN F and JACOBSON G. Roentgenographic diagnosis of small amounts of intraperitoneal fluid. *Amer J Roentgenol* 99 (1967) 62.
- FARM DARR J. Roentgen examinations in acute abdominal diseases. Second edition. Charles C. Thomas, Springfield, Illinois 1960.
- The acute abdomen. *J. Encyclopedia of medical radiology*, p. 447. Springer Verlag, Berlin Heidelberg New York 1968.
- GIERA J, JORLIE H and LIVADITIS A. Management of intussusception. A survey based on 288 consecutive cases. *Pediatrics* 50 (1972) 535.
- JORLIE H. Roentgen diagnosis of small amounts of intraperitoneal fluid. To be published in *Acta radiol. Diagnosis*.
- LAJTHI H. Roentgen symptoms in abdominal discharges. *Acta radiol* 4 (1925) 63.
- Röntgenologische Zeichen abdomineller Ergüsse. Zugleich ein Beitrag zur Röntgendiagnostik der Intussuscat. *Acta radiol* 5 (1926) 63.
- (a) Über die Lagerung, von freier Flüssigkeit, freiem Gas und beweglichen Gasgeblähen im Darmen in der Bauchhöhle. *Acta radiol* 8 (1927) 109.
- (b) Über die Röntgensymptome bei einem Fall von intra- und retroperitonealer Entzündung und über frühe röntgenologische Zeichen der akuten Osteomyelitis. *Acta radiol* 8 (1927) 289.
- MARGULIES M and STOLAR L. Hepatic angle in roentgen evaluation of peritoneal fluid. *Radiology* 88 (1967) 51.
- SCHATZKI R. The roentgenologic appearance of intussuscepted tumors of the colon with and without barium examination. *Amer J Roentgenol* 41 (1939) 549.

THE DIAZO METHOD

A simplified method of preparing multicolor combination images
for use in roentgen diagnosis

S EKLUND L JENSRATT B SCHAMPI and U WELANDER

There are many cases in routine roentgenographic work, in which diagnostically valuable information is represented by differences in the appearance of the image in two or more roentgenograms of the same object. In order to be able to judge whether a lesion is undergoing regression, has remained unchanged, or is progressing, comparisons must be made between different roentgen images. Another example of this is the varying information recorded in the different component views in a serial examination of a dynamic sequence, as in angiography. In the majority of such cases each separate image is assessed subjectively. Measurements may sometimes be made on the films themselves and at others tracing with the aid of a transparent film on which individual details in the images are sketched and then compared in the different films is of value. It would however be advantageous to be able to carry out the assessment on a single image; this is in fact, possible in certain cases.

If copies of the originals in a roentgenologic series of films be prepared in different colors the images can be combined into a composite multicolor combination image. The differences between the component views will then be presented visually in the combination image as changes in color. Before in-

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dividual detail in the films can be investigated with this technique the component view must have been exposed in exactly the same projection. This requirement may be fulfilled with rapid sequences in which the examination can be carried out within a limited time. ILLIFQUIST & WELANDER (1969) have presented a method for preparing multicolor combination images and WELANDER in the same year published a more detailed description of the technique.

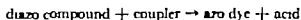
WELANDER has also analyzed the principles for interpreting this type of image. The method has been used for the assessment of rapid serial angiographies. The combination images provide in some cases increased information regarding both anatomic detail in the vascular system and the circulatory conditions.

ILLIFQUIST & WELANDER 1969, 1970, WELANDER 1969 (Fig. 1).

The color film were previously prepared with Kodachrome developers but as this method is complicated and time consuming various color processing techniques have been tried with a view to simplifying it and making it more suitable for routine work. The simplest method for preparing multicolor combination images seems at present to be to utilize the diazotype process (MULLER 1942, MUTTER 1963, COFFMAN).

The diazotype process. The diazotype process is a printing technique that is being increasingly used for reproducing color images and is based on the diazo compounds discovered by GRIFFS in 1838. These are benzene derived organic compounds in which one of the hydrogen atoms in the benzene ring has been replaced by two atoms of nitrogen — hence the name diazo. They are prepared by treating aromatic primary amines with sodium nitrite and acid.

Diazo compounds can be used in the manufacture of dyestuffs. In the presence of an alkaline agent such as ammonia they react with certain other organic compounds to form azo dyes. The latter compounds usually consist of phenols or aromatic amines, and are generally known as coupler components or couplers. In outline the formation of azo dyes takes place in the following way:



Various colors depending upon the choice of coupler may be produced.

WEST as early as 1885 found that the diazo compounds are light sensitive — a discovery that set in train the developments that have led to the diazotype processes in use today. When a diazo is exposed to ultraviolet light the two nitrogen atoms are knocked out of the benzene ring leaving a phenol which is incapable of reacting with the coupler component to form a dye. If an emulsion of a diazo and a coupler component, be applied on a suitable base an ultra violet light sensitive film will be obtained and can be developed in the presence

of an alkaline agent. Unexposed parts will be developed and in contact prints the film thus gives a positive image of the original.

The authors used a film with a light sensitive layer including a coupler component on a plastic base and intended for development in ammonia fumes. The emulsion is grainless and the film base is transparent. Films are available in a large number of colors. The practical printing work is simple. A printing machine with a high intensity of ultraviolet radiation permits short exposure times and the developing process takes only 1 to 1.5 minutes. The print is ready immediately after development, no fixation or other treatment of the film is necessary and it remains dry throughout.

The diazotype process is used mainly in the printing industry. Properties that are acceptable or desirable in those contexts may however cause difficulties when the method is used in the preparation of multicolor combination images. No satisfactory information is available regarding the power of the diazo films to transmit different wavelength ranges or regarding their color density and gradation. It was therefore of interest to investigate the films from the aspect of the special problems connected with their use in the preparation of multicolor combination images. The object of the tests was to ascertain whether the diazo method may be used for obtaining combination images. If this question could be answered in the affirmative it was hoped to increase the technical efficiency of the work of reproduction of combination images and to investigate the special characteristics of the diazo combination images with respect to gradation, color density and color.

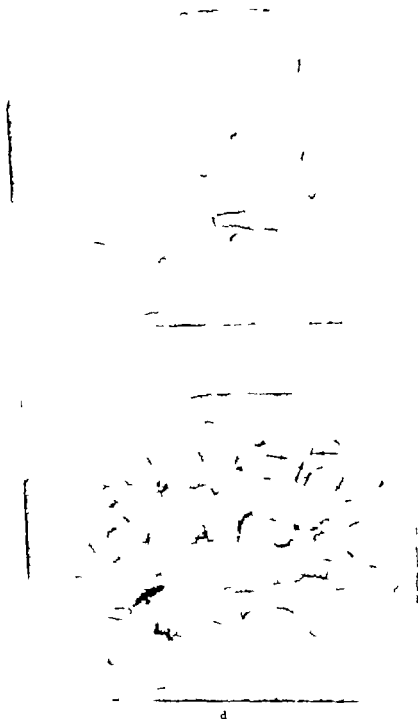
Authors' investigation

Diazo films in the subtractive primary colors were used for the tests. Density curves with the density placed in relation to the relative exposure were compiled to investigate the gradation, latitude and color density of the films. The power of the films to reproduce the differences in density in an original film was also examined. It is necessary to have this information regarding the diazo films in order to be able to utilize their properties to the full when carrying out the technical work of preparing a multicolor combination image. A knowledge of the gradation and latitude is also needed for the interpretation of the final image, each time an original image is processed changes may occur in the information contained in the image and it is therefore important to know what alterations may be expected when an original image is converted into a diazo print.

The films were finally investigated from the aspect of their transmission of different wavelength ranges. Monochromatic color filters filter transmitted light selectively. With a combination in pairs that part of the spectrum common



FIG. 1. Retrograde filling of parietal branch of the middle cerebral artery. The retrograde circulation may be readily detected in the multicolor combination image because the color scale is reversed. The pathologic direction of flow is difficult to distinguish in the black and white original subtraction film. Circulatory disturbances also exist in the posterior cerebral artery.



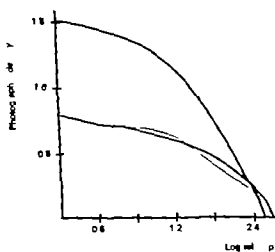


Fig 2 Color density curves for yellow magenta and cyan diazo films

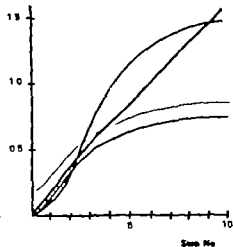


Fig 3 Reproduction of the different densities of a gray scale by yellow magenta and cyan diazo films

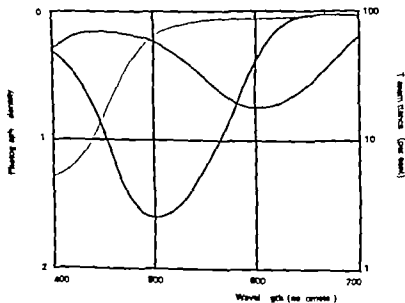


Fig 4 Transmission diagrams for yellow magenta and cyan diazo films

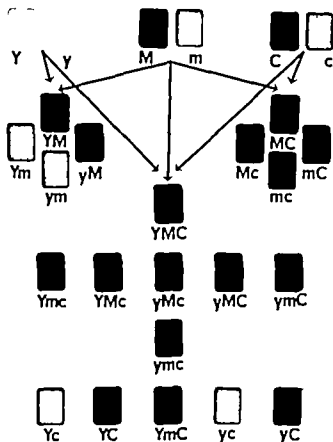


Fig. Schematic representation of colors produced with various mixtures of yellow, magenta and cyan with two different degrees of color density (Y, M and C, and y, m and c). The lower greenish tones would not be logical combination assures that present continuous sequence.

to both filters is transmitted this selective transmission of different regions of the spectrum causes the color shifts evident in a multicolor combination image. The three monochromatic component films thus act as color filters and consequently a knowledge of their transmitting properties is essential for assessing the color changes that appear in the combination image.

Method The tests were carried out on Tecnifax Diazochrome film (Tecnifax Corporation Holyoke, Massachusetts USA) KYL (yellow) KMG (magenta) and KCY (cyan). The films were stored in accordance with the manufacturer's instructions — in the dark, in a cool temperature (about 10 °C) and without risk of exposure to ammonia fumes. After the printing process, they were kept in the dark. Direct sunlight and ultraviolet illumination were avoided.

The printing work was done in a printer Oce 14 which gives even ultraviolet illumination and is equipped with a timer. The exposure time was varied according to the density of the original film and the color density desired in the print. As different diazo films including those with different colors but of the same make vary in sensitivity the exposure times had to be suitably altered.

After printing the prints were developed in a box developer designed by the authors and made of plexiglas and provided with a removable close fitting lid. The film hung free attached to metal clips, and the ammonia fumes were generated from a layer of 20 % ammoniac poured onto the bottom of the box. Development was carried out under standardized conditions at room temperature. More effective vaporization and a shorter development time may be achieved by heating the ammoniac.

The color density curve Strips of the three diazo films were fed along step by step so that exposure of the unexposed parts of the film took place successively. All exposure factors were constant: the exposure time at each forward feeding movement was 4 seconds. Strips were thus obtained that had been gradually exposed for 0 to 100 seconds.

Density reproduction A standardized gray scale, Kodak Photographic Step Tablet No 3 with nominal density increment 0.15 and nominal density range 0.05 to 3.05 was printed on the three films. The exposure times were adjusted so that the lowest densities in the gray scale would be distinguishable while areas to the side of it were completely colorless.

All the strips both those to be used for color density curves and those intended for investigation of density reproduction, were measured in a McBeth color densitometer with filters in the complementary color of the respective

drazo film: a blue filter was used for yellow, a green filter for magenta, and a red filter for cyan.

Transmission. Unexposed films in the three colors underwent standardized development to maximum density, and the transmission was measured in a Beckman spectrophotometer.

Results

The color density curve. Drazo films fade on exposure, and the density curves are therefore reversed in comparison with the density curve of a conventional film (Fig. 2).

There was no sign of any threshold value that had to be exceeded before the exposure would result in incipient decolorization of the drazo film. The curves for all the colors were, however, flattened in the initial part of their course, indicating that the coloring decreased relatively slowly at first with increasing exposure. On further exposure the density curve became steeper and finally corresponded approximately to a value of 1 for yellow and cyan films, while the magenta film had a slightly higher value. The curves ended abruptly at the 0 density. There was thus no asymptotic part in the curves for the drazo film.

The maximum color density was relatively low for all three drazo films: about 1.5 for magenta and about 0.8 for cyan and yellow.

Density reproduction. The results of the measurements for the strips exposed with a standardized gray scale are illustrated diagrammatically in figure 3, where the straight line marks the gradually increasing density of the gray scale.

All the drazo films reproduced the density of the original film almost perfectly in the parts of the gray scale with low density. The color density of the drazo films rose steeply at first and followed more or less completely the density of the gray scale; the value of the films thus corresponded approximately to 1 in the areas with weak coloring. In those areas of the gray scale in which the density was higher, the coloring of the drazo films leveled out, and areas of very high density were reproduced with constant maximum coloring for the respective drazo film.

Transmission. The transmission curves for the drazo films tested are given in Figure 4.

The ideal color filters in the subtractive primary colors should have the following properties:

	blue	green	red
	400—500	500—600	600—700
	nanometer	nanometer	nanometer
yellow filter	absorption	transmission	transmission
magenta filter	transmission	absorption	transmission
cyan filter	transmission	transmission	absorption

Transmission and absorption are total in the theoretically ideal case. There are no filters with these properties; the maximum and minimum transmission however must be in agreement with this tabulation.

The properties of the diazo films as color filters in the subtractive primary colors are evident in the transmission diagram. The yellow film presented a high degree of green and red transmission although more absorption in the blue region of the spectrum would have been desirable. The magenta film transmitted red to a maximum and blue well; the minimum transmission was at approximately 500 nanometer corresponding roughly to the transition between the blue and green ranges in the spectrum. The magenta film would have come closer to the ideal if the transmission minimum had lain slightly towards the right in the diagram between 500 and 600 nanometer and if the blue transmission had been as high as that of the red. It could be said that the magenta film was more red than an ideal magenta colored filter. The cyan film had its transmission maximum in the blue range and its minimum in the yellow range — about 600 nanometers. The transmission of green and red was approximately equal. The transmission minimum would ideally be shifted towards the right in the diagram and would lie within the red region of the spectrum; the transmission of green would also be higher. The cyan film was more blue than the ideal cyan colored filter.

It could be said of all three diazo films that without being perfect color filters they nevertheless corresponded on the whole to filters in the subtractive primary colors.

Discussion

The maximum color density in the three diazo films was relatively low although this is not a disadvantage in the preparation of combination images; in the combined image the color density in three component films is summated and the low density of the diazo films is both an advantage and a prerequisite in ensuring that the total maximum density will not be too high. Differences in color density within the object are of minor significance in the interpretation of combination images; the factor that is associated is the color shifts, and these

are optimal only when the component images in the combination have low density.

The abrupt termination of the density curves without any asymptotic continuation is a great advantage when prints on diazo films are being prepared. In films with that property the conditions for obtaining a correct print of the most delicate parts of an original image, namely areas of lowest density, are extremely advantageous.

The subtraction films that are to be printed on diazo film should reproduce the skeletal structures evenly and completely; the skeleton must be distinguishable but only in very low density. If this requirement be met, all contrast-filled blood vessels will be depicted in the subtraction image; the density of the vessels is always higher than that of the skeleton. The advantageous part of the density curve of the diazo film where $D = 1$ will be utilized when the density of the subtraction image is low.

The entire density range in those parts of a subtraction image that have high density is reproduced in diazo prints with constant maximum color density. However, differences in the density are of minor significance when a combination image is being assessed, and this factor need have no effect on the information contained in the image. Nor is the information content affected by the higher maximum density in the magenta film.

The transmitting properties of the three diazo films were very satisfactory from the practical point of view; the films showed good correspondence with color filters in the subtractive primary colors. However, when the diazo films were combined in pairs, shifting of the intermediate colors occurred as compared with combinations in pairs of the ideal subtractive primary colors. Such color shifts were most noticeable when cyan and magenta were combined. This combination results in blue in the ideal case, but when the diazo films were combined it was blue-red (mauve) owing to the transmission properties of the films.

Although the deviations from the ideal primary colors evident in diazo films are of minor significance in the preparation and assessment of multicolor combination images, it is absolutely necessary to appreciate them and to know what color changes arise in combinations of diazo films. Figure 5 is a schematic illustration of the colors that arise on combination of yellow, magenta, and cyan with the properties possessed by the diazo films. The figure also depicts the color changes that are due to varying color density as exemplified by two different degrees of density.

Diazotype materials are fairly sensitive to physical or chemical action. Unexposed films must be kept cool and dry, and should not be exposed to the action of alkaline substances. Diazo films may be handled in a lighted room.

but should not be exposed to ultraviolet illumination from neon lights, nor to daylight. Even when stored under ideal conditions, diazo films sometimes present local color imbalance; the quality does not seem to be wholly constant.

Exposed diazo films are bleached by light — slowly by artificial illumination and fairly rapidly by sunlight. However, if the films are stored in the dark, the shelf life is very good.

The eye's ability to see color is complicated and cannot be measured by objective methods. As a consequence, the data concerning diazo films presented in this paper are not wholly adequate since consideration must also be paid to the psychophysiologic mechanisms that underlie the faculty of vision. However, to the extent that it was possible to carry out an objective analysis, diazo films proved satisfactory from both the technical and the practical points of view for the preparation of multicolor combination images. The method is simple and the films may be quickly prepared.

Conclusions

1) The properties of the diazo films both as regards the color density curve and the power to reproduce the densities of an original film were such that they could be considered suitable for use in the preparation of multicolor combination images.

2) The color filtering qualities of the diazo films were from the technical viewpoint satisfactory for the production and assessment of multicolor combination images.

SUMMARY

The roentgenologic application of multicolor combination images is described. The technical and qualitative properties of a special brand of diazo film in the subtractive primary colors were examined and found to be suitable for the preparation of such images.

ZUSAMMENFASSUNG

Die Röntgenologische Anwendung von Mehrfarb-Kombinationsbildern wird beschrieben. Die technischen und qualitativen Eigenschaften einer besonderen Art von Diazo-Films in den subtraktiven primären Farben wurde geprüft und als geeignet für die Herstellung von solchen Bildern befunden.

RÉSUMÉ

Description de l'application radiologique d'une combinaison d'images multicolores. Les auteurs ont étudié les propriétés techniques et qualitatives d'un type spécial de film diazo pour les couleurs primaires soustractives et ont trouvé qu'il convient pour la préparation de ces images.

REFERENCES

- CORREIA, J. W. Technology of the diapositive process. Tech. Lit. Corporation, Hothoke, Massachusetts.
- LAURENSEN, B. and WELANDER, U. Colour in subtraction angiography. Preliminary report. *Acta radiol. Diagnosc.* 8 (1969) 1.
- Colour combination images in cerebral angiography. *Neuroendocrinology* 1 (1970) 37.
- NEITZ, I. Kompendium der Lithographie. Verlag für Radio-Photo-Kameratechnik GmbH, Berlin-Borsigwalde (1961).
- MILLER, F. R. Diatypes: principles. In: *Fotografisk handbok*, Kap. 81. (In Swedish). Edited by H. B. Åström. Natur & Kult., Stockholm (1972).
- WELANDER, U. Multicolor combination images in subtraction angiography. A new photographic method and its applications. *Acta radiol.* (1969) 5 pp. No. 790.

CINEANGIOGRAPHIC ESTIMATION OF THE LEFT VENTRICULAR VOLUME DURING ACUTE MYOCARDIAL ISCHAEMIA IN DOGS

N E AHLBERG L FRANKEMO MARIA LINDFORS and T SEPMAN

The total heart volume calculated from the cardiac contour in the roentgenogram (HAHLSTOFF 1932 LILJESTRAND et coll 1939 JOYSELL 1939 BERGSTROM et coll 1969) must be supplemented by the measurement of the volume of an atrium or ventricle if a correct estimation of cardiac function be required. The volume of the left ventricle may be obtained by different methods, e.g. angiography and scintigraphic techniques or direct measurements of the volume flow of blood. Methods of estimating the left ventricular volume by cineangiography have been described by DODGE & TANNENBAUM (1956) and by cineangiography by CHAPMAN et coll (1958) and GRIBBE (1960) techniques that have later been modified (ARVIDSSON 1961 HERMANN & BARTLE 1968).

Most methods are based on the assumption that the left ventricle in both end diastol and end systole may be approximated to the shape of an ellipsoid body and the volume therefore calculated by the formula of this geometric figure.

Moreover some authors have indicated that the volume of the left ventricle may thus be calculated with almost the same accuracy from single as from

biplane cineangiography (GREEN *et coll.* 1967, SANDLER & DODGE 1968, KASSER & KENNEDY 1969). The ventricular volumes obtained from angiograms by the ellipsoid formula have also correlated well to those determined by the indicator dilution technique or by measurements of phasic areas of the chambers (CRIBBE 1960, DAVILA & SANMARCO 1966).

The angiographic methods therefore seem to provide a practical approach to the measurement of the ventricular volume provided that the heart has a normal shape and movement. However immediately after coronary occlusion the shape and movement of the ventricle change characteristically (LENNART & WIGGERS 1935, AHLBERG *et coll.* 1972). The contractility of the ischaemic region of the myocardium is altered which at least in systole produces marked distortion of the ventricular chamber. It is therefore not at all clear that this cavity may in myocardial ischaemia be likened to a symmetric geometric figure such as an ellipsoid.

The present investigation was undertaken to obtain a more accurate method for estimating the volume of the ventricle when changes in its shape and movement due to myocardial ischaemia are present. The ventricular volumes were calculated from cineangiograms with a new technique and compared with the values derived from the ellipsoid method. The values calculated for stroke volumes were compared to those obtained by square wave electromagnetic flow meter and dye dilution techniques.

Theoretic considerations. The shape and movement of the ventricle during myocardial ischaemia is not uniform (AHLBERG *et coll.* 1972). If the cavity of the ventricle however be assumed to be circular in cross section and the ventricle to curve only in one projection the volume may be calculated as follows. The left ventricular cavity is regarded as a mathematical three dimensional body swept by a circular area whose diameter varies as it moves with its center along a curved line: this area must always be perpendicular to the central line and pass once and once only through each point of the region swept (Fig. 1 a). The curved line ($O-S$) is called the left ventricular midline and is formed by the central point of the moving circular area with diameter (l) sweeping over the projected chamber perpendicular to the midline. The square values of the diameter (l) may be expressed as a function of the arch length (s) of the midline and represented graphically in a coordinate system (Fig. 1 b). By definition of integral the area of this figure must be

$$A = \int_0^{S_0} l^2(s) ds \quad (1)$$

In the three dimensional body where (l) is the diameter in the circular area moving along the arch length (s) the volume of the body will be (COURANT 1959)

$$v = \frac{\pi}{4} \sum_0^s l(s) ds \quad (2)$$

From this the volume of the body may also be expressed as

$$v = \frac{\pi}{4} A \quad (3)$$

The area (A) in the coordinate system (Fig 1 b) may be estimated with a planimeter thus affording a means of calculating the volume

Only small discrepancies in shape exist between the mathematical model and the ventricular cavity in the projection used. This occurs particularly in the basal part of the chamber or in the deformed ischaemic part during coronary occlusion (Fig 3 a). This means that the left ventricular midline is not always perpendicular to the moving area if the latter should pass only once through each point. However formula (2) may be corrected if the moving area should not be perpendicular to the midline by replacing $l(s)$ with $l(s) \cos \alpha$ where α is the angle between the moving area and the normal plane of the midline. These deviations are judged to be negligible in the volume estimations since $\cos \alpha$ is close to 1 and the corresponding sections of the midline are short. The estimation of the left ventricular volume from the cineangiograms thus seems to be possible if the above two assumptions be allowed. A special investigation with a biplane cineangiographic technique was therefore undertaken to determine whether the ventricular midline may be approximated to a straight line in the projection perpendicular to the one used and the cross section area of the chamber approximated to a circle.

Material and Methods The material consisted of 11 dogs 15 to 25 kg in weight, anaesthetized by intravenous pentobarbital and curare and ventilated artificially. The heart was exposed by left thoracotomy, and a short section of the left anterior descending coronary artery dissected for subsequent occlusion with a snare (JOHANSSON et coll 1964 1965 LINDEN 1966). A metallic indicator was sutured to the epicardium centrally in the expected ischaemic area so as to facilitate proper identification and positioning of this area in the radiographic recording system. The pericardium and thorax were then closed with the snare through the chest wall for subsequent occlusion.

The cineangiographic examinations were performed directly following the operation, 35 mm Arriflex cameras with cine pulse and 9 inch image intensifiers being employed. The animal was placed on the left side slightly tilted so that the area of the left ventricle marked by the metallic indicator was depicted tangentially by the vertical roentgen beam. This projection was almost identical with that in which the long axis of the left ventricle lies perpendicular to the direction

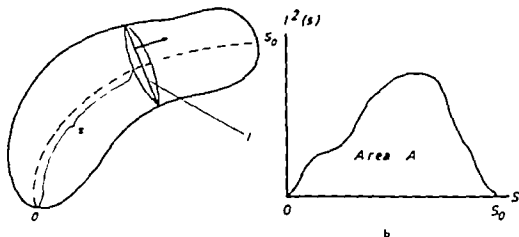


Fig. 1. A three-dimensional body concept (left) and the diameter (l) of which axes (in cm) with its centre (right) curved line ($0 \leq s \leq l$). The square values of the diameter l expressed as a function of the arch length (s) of the outline and represented in co-ordinate system.

of the roentgen beam. The tube film and object film distance were constant in all experiments. The angiographies were performed with injections of contrast medium into the left atrium with a power injector (Caval I-Ekman-Schneider) and a film speed of 60 or 70 frames per second.

One to three temporary occlusions were performed in each animal and the effect on the myocardial wall was then observed with repeated cineangiographic recordings. Cineangiography was carried out in 4 animals in two projections simultaneously, one of these with the previously described vertical and the other with horizontal roentgen beam. In the other 7 animals single films were taken in the latter projection only to control the position of the ventricle in relation to the projection of the single plane cineangiograms.

The cineangiography in 5 dogs was combined with simultaneous measurements of cardiac output both with a square wave electromagnetic flow meter (Alicon) and with a dye dilution technique with indocyanine green (Cardio-Green, Hynson, Westcott & Dunning) and the Beckman Cardio-Densitometer apparatus. The ascending aortic flow was taken as an indication of cardiac output and a flow probe of a size to fit the vessel snugly was placed around the aortic root. The flowmeter was calibrated *in vitro* using an excised vessel. Zero flow for mean blood flow *in vivo* was obtained by shutting off the probe magnet. The diastolic quiet interval when no flow except coronary flow occurred in the aorta was used as a measure of zero value for peak flow (Sjöström & Dedering 1967). The stroke volumes were estimated planimetrically from the peak flow curves. The cardiac output immediately before each film sequence was determined by the dye



Fig. Cineangiography a) End systole b) End diastole

dilution technique. The indicator dye (125 mg Cardio-Green in 0.5 ml volume) was injected into the right atrium through a catheter inserted via the femoral vein. Arterial blood was withdrawn from a catheter inserted in the femoral artery by means of a motorized syringe working at constant speed. After each flow measurement the blood was reinfused, individual calibrations being performed for every dog with three different dilutions of the indicator dye and a blank sample.

The cineangiograms were examined in a projector (Tagarno) with frame analyses up to a speed of 24 frames/s, each frame being projected onto a screen that permitted contour tracing. The images of the well filled left ventricle were traced for one to three heart cycles and from the frames corresponding to end diastole and end systole the estimations of volume were performed. End-diastole was chosen as the image that preceded immediately the closure of the mitral valve and the frame immediately before the closure of the aortic valve was selected to represent end systole. The closed valves were identified in the frames and the apex and the base point of the ventricular cavity defined; the base point was identified as the transition between the aortic and the mitral valves.

The frames from both single and biplane angiography were handled as follows. The ventricular midline was drawn from the base point to the apex and the diameters perpendicular to this were constructed at a distance of 0.5 cm. The course of the ventricular midline was examined from simultaneous biplane frames; in addition the corresponding apical, central and basal diameters and the mean values of all those measured in the images of the ventricular cavity were compared in the two projections in simultaneous frames.



Fig. 3. Cineangiographic tracings of the left ventricle end-systole and end-diastole respectively. (a) With the midline and the diameters constructed by the model method. (b) With the long axis L constructed.

The ventricular volumes were calculated by the model method in the frames from the single plane series (Figs 2, 3 a). The lengths of the diameters squared were plotted on the ordinate and the length of the ventricular midline on the abscissa with the base point at the origin (Fig. 1 b). The area of the constructed figure in the coordinate system was then estimated with a planimeter and using formula 3 the volume was estimated.

The frames were also used for the calculation of the ventricular volume by the method of approximating the ventricle to an ellipsoid figure (HASSER & KENNEDY 1969). A straight line was drawn from the base point to the apex (Fig. 3 b) and the length of this long axis (L) measured (cm). The area of the ventricular chamber (T) was measured (cm²) with a planimeter. The volume was then given by the formula:

$$V = \frac{8T^2}{3\pi L} \quad (4)$$

Correction for magnification was made with a fine meshed metal grid filmed in both projections in the same position as the heart. The same correction factor of 0.735 was used for all the single plane series with separate factors for correction of the biplane series. Pin cushion distortion peripherally in the image amplifier was slight and therefore needed no compensation. The angle between the long axis of the left ventricle and the horizontal plane was measured in the single roentgen images and corrected for in the estimation of the volumes.

The stroke volume was calculated as the difference between the estimated volume in end-diastole and in end-systole and directly measured from the simultaneously registered peak electromagnetic blood flow curve. Cardiac output obtained by the dilution technique was compared to electromagnetic mean flow or cardiac output calculated as peak flow times rate but not directly to the values from the cineangiogram due to the error in the dye dilution caused by the injection of contrast medium.



Fig 4 The left ventricle midline in end diastole (—) and end systole (---) constructed on tracings with horizontal roentgen beam direction before and during occlusion of the left anterior descending coronary artery

Results

Biplane cineangiography The shape of the left ventricular chamber in end diastole was almost identical in the two projections and failed to change during coronary occlusion. The ventricular midline in both projections was almost straight. The shape in end systole differed in the vertical and horizontal projections a difference that was more marked during myocardial ischaemia. The ventricular midline in the plane obtained with the vertical roentgen beam was then curved but the midline in the perpendicular plane was almost straight (Fig 4). There were generally small differences between the corresponding diameters from the vertical and horizontal projections (Fig 5) but the mean values of the diameters in 48 calculations correlated well both in end diastole (2.94 cm SD 0.51 and 2.90 cm SD 0.61 respectively $r=0.94$) and end systole (1.91 cm SD 0.51 and 1.98 cm SD 0.59 respectively $r=0.94$) before and during coronary occlusion.

Single plane cineangiography The volumes of the left ventricle were calculated from the frames obtained with the vertical roentgen beam in 7 dogs before and during coronary occlusion. In end diastole where the ventricular cavity had an ellipsoid shape good correlation existed between the volumes calculated from the model method and the conventional ellipsoid method before and during coronary occlusion (Fig 6a). In end systole however the shape of the cavity differed from an ellipsoid especially during coronary occlusion when it became pear or club-shaped (Fig 2). This may explain the impaired correlation between the volumes at end systole calculated with both methods when marked ischaemic changes in the ventricular shape were present (Fig 6b).

The cardiac output measured by the dye dilution technique in 22 calculations was 2.28 l (SD 0.77) and 2.11 l (SD 0.79) with the electromagnetic flowmeter. The values of the two methods correlated well ($r=0.98$). The stroke volumes

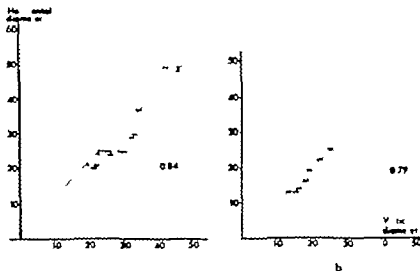


Fig. 5. Correlations between corresponding pical, entral and basal diameters in erect and horizontal projections from simultaneously exposed cineangiograms. Values from end-diastole (a) and end-systole (b) both before and during occlusion of the left anterior descending coronary artery.

calculated from the cineangiograms with the ellipsoid and the model methods also correlated well ($r = 0.92$ and 0.94 respectively) with those estimated electromagnetically (14.68 ml SD 5.7, 14.41 ml SD 5.4 and 15.04 ml SD 5.6 respectively). It was obvious, however, that the ellipsoid method gave somewhat lower values for the stroke volumes when the ventricular shape was markedly changed during coronary artery occlusion (Fig. 7). As the volumes in end-diastole correlated well with the two angiographic methods, this deviation may be due to a tendency to overestimate the volumes in end-systole with the ellipsoid method but not with the model method (Fig. 6b).

Discussion

Normally the shape of the left ventricular cavity varies so widely during the cardiac cycle that it hardly can be looked upon as the same geometric figure. It is therefore questionable if the expectations attached to the commonly used angiographic methods for volume estimations are justified, as all of these mean an approximation. Methods based on the principle to approximate the ventricular cavity to an ellipsoid have however been useful in clinical practice and correlate well with other methods for estimation of cardiac output (GARNER 1960, ARVIDSSON 1961). It has to be pointed out that this ellipsoid method implies an error in estimation of end-systolic volumes even during normal conditions.

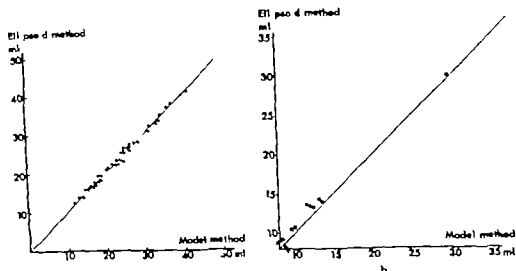


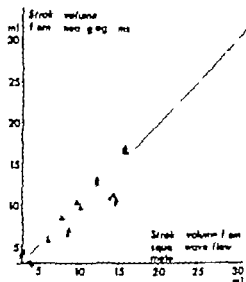
Fig. 6 Correlations between the values of the left ventricular volume calculated in the ellipsoid and model methods in the same cineangiogram. a) In end diastol before and during coronary occlusion. b) In end systole during occlusion of the left anterior descending coronary artery.

During acute myocardial ischaemia however the shape of the ventricular chamber changes so much that the resemblance to an ellipsoid is completely lost (AHLBERG *et coll* 1972).

The ideal cardioangiographic method for the estimation of the ventricular volume should be independent of its shape. Methods such as different applications of Simpson's parabolic rule (CHAPMAN *et coll* 1958) or the Styrofoam model method (CARLSSON 1966) are complicated and time consuming and have been of little value. The employment of a cardioangiographic method that compensates for pathologic shapes of the ventricular chamber therefore appears justified even if this implies some approximations. Objections may be raised to the uncertainty of the effects of the sudden injection of contrast medium, the agent itself or the varying degrees of ventricular filling produced: these will however be valid for all angiographic methods.

The model method is valid only provided the cross-section of the ventricular cavity can be approximated to a circle and curves mainly in one plane. Earlier investigations (DODGE *et coll* 1960, GREENE *et coll* 1967) have presented good correlation between corresponding diameters in perpendicular planes of the ventricle in man. The corresponding diameters in the present investigation differed moderately in the two projections while the mean values were correlated

Fig. 3. Relations between stroke volumes calculated from the cineangiographic frames with the model (Δ) and ellipsoid (\bullet) method and estimated by a square wave flow meter during occlusion of the left anterior descending coronary artery.



most satisfactorily. The assumption that the cross-section of the left ventricular cavity is a circle thus cannot be proved, but if the approximation still be made, the error of local non-circularity must be considerably reduced because of the close correlation of the mean diameters. The other assumption that the ventricular cavity curves mainly in one plane must also be accepted for the ventricular midline in the perpendicular projection, as in Fig. 4, was almost straight. The projection used for this single plane angiography centrally through the ischaemic region must therefore be the optimal one. Objections may be raised that it will be difficult in clinical practice to determine this optimal projection through an ischaemic region. However, even if the deviation from the ideal projection produces an error in the volume calculation which will be greatest in a plane perpendicular to the ideal one, this error will still be less than or equal to that with the ellipsoid method.

Calculation of the ventricular volume with the model method from frames obtained in the ideal projections thus seems to produce values almost identical to the true ventricular volume, even in pathologic condition. This assumption is supported by the result from measurements of the stroke volume with the electromagnetic flow meter and by measurements of the cardiac output with the dye dilution technique. However, some of the values from volume calculation with the ellipsoid method also appear to correlate well with the flow values. The question therefore arises as to whether the model method really signifies an advantage over the other method. The values from the model and ellipsoid

methods correspond well at end diastole both before and during coronary occlusion (Fig. 6 a). This, however, must be due to the fact that the ventricle in end diastole assumes an almost ellipsoid form even during coronary occlusion (AHLBERG et coll. 1972). On the other hand this shape is no longer apparent during occlusion in end systole. As the model method compensates for this change the calculation of the ventricular volume must be more accurate. Furthermore the blood flow estimations seemed to be better correlated to the values from the model method than from the ellipsoid method when the shape of the ventricular chamber was much changed during acute coronary occlusion. The advantages of the method presented thus seem to be that estimations of the left ventricular volume may be performed in different phases of the heart cycle with sufficient precision to evaluate changes in the heart even when the left ventricular chamber is deformed.

Acknowledgement

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SUMMARY

A method of estimating left ventricular volume with single plane cineangiography has been introduced and compared with an ellipsoid method in dogs. Left ventricular stroke volume and cardiac output were estimated simultaneously with a square wave electromagnetic flow meter and by dilution technique before and during occlusion of the left anterior descending coronary artery. The correlations between the methods are discussed.

ZUSAMMENFASSUNG

Eine Methode der Bestimmung des Volumens des linken Ventrikels durch Filmangiographie in einer Ebene wurde eingeführt und mit einer Ellipsoid-Methode an Hunden verglichen. Das Schlagvolumen des linken Ventrikels und das Minutenvolumen wurden gleichzeitig mit einem verfahren ellipsoiden elektromagnetischen Strömungsmeter und der Farbstoff-Verdünnungstechnik vor und nach Verschluss der linken Herzkranzarterie bestimmt. Die Korrelationen zwischen diesen Methoden werden diskutiert.

RESUMÉ

Les auteurs présentent une méthode de détermination du volume ventriculaire gauche au moyen d'une cinéangiographie unidirectionnelle et la comparent au des chlorure à une méthode qui assume l'entricule à un ellipsoïde. Le volume d'injection ventriculaire gauche et le débit cardiaque ont été mesurés simultanément au moyen d'un débitmètre électromagnétique indirect et par la technique de dilution de colorant à haut débit pendant l'abaissement de l'artère coronaire descendante antérieure gauche. Les auteurs examinent les corrélations entre ces méthodes.

REFERENCES

- ALLEN, N. E., J. A. LINDSAY and SPEMAN, T. Left ventricular changes during coronary artery ligation in dogs. *Acta radiol. (Diagnos.)* 12 (1971) 789.
- ANDERSON, H. An angiocardigraphic determination of left ventricular volume. *Acta radiol.* 36 (1961) 1.
- BERGSTRÖM, K., BACKLUND, L., FRANKLIN, L. and CRYSTENSON, B. Heart volume and relation to measures of circulatory function in healthy young men. *Acta med. scand.* 183 (1968) 41.
- CARLISLE, I. Angiocardiographic measurement of the cardiac ventricles in dogs. *Acta radiol. (Diagnos.)* 4 (1966) 671.
- CHAMBERLAIN, C. B., BAKER, O., REYNOLDS, J. and BONTÉ, F. J. Use of biplane cinefluorography for measurement of ventricular volume. *Circulation* 18 (1958) 1105.
- COCHRAN, R. Differential and integral calculus. Blackie and Son, London, 1953.
- DANIEL, J. C. and SAMMARCO, M. E. An analysis of the fit of mathematical models applicable to the measurement of left ventricular volume. *Amer. J. Cardiol.* 18 (1966) 31.
- DODGE, H. T. and TAMMAM, H. L. Left ventricular volume in normal man and alterations in disease. *Circulation* 14 (1956) 927.
- , SANDLER, H., BAILEY, D. W. and LORD, J. D. The use of biplane angiocardiography for the measurement of left ventricular volume in man. *Amer. Heart J.* 60 (1960) 762.
- GREENE, D. C., CARLISLE, R., GRANT, C. and BUNNELL, I. L. Estimation of left ventricular volume by one plane cineangiography. *Circulation* 35 (1967) 61.
- GRUBB, P. Comparison of the angiocardiographic and the direct Fick methods in determining cardiac output. *Cardiologia* 36 (1960) 20.
- HERMANN, H. J. and BARTLEY, H. H. Left ventricular volumes by angiocardiography. Comparison of methods and simplification of technique. *Cardiovasc. Res.* 4 (1968) 404.
- JONSSON, B., LINDER, E. and SPEMAN, T. Collateral blood flow in the myocardium indirectly measured with krypton. *Acta physiol. scand.* 62 (1964) 263.
- , —, —. Coronary collateral blood flow in relation to the mass of ischemic myocardium studied with krypton. *Acta physiol. scand.* 63 (1965) 493.
- JONWELL, S. A method for the determination of the heart size by teleroentgenography (heart volume index). *Acta radiol.* 20 (1939) 32.
- KÄHLSTEDT, A. Über eine orthodiagraphische Herzvolumenbestimmung. *Fortschr. Röntgenstr.* 42 (1932) 123.
- KAMRÉ, J. S. and KENNEDY, J. W. Measurement of left ventricular volumes in man by single-plane cineangiography. *Invest. Radiol.* 4 (1969) 83.
- LEIJERFELT, G., LINDGREN, E., NYLIN, G. and ZACHARIUS, C. The normal heart volume in man. *Amer. Heart J.* 17 (1939) 406.

- LINDER F. Measurements of normal and collateral coronary blood flow by flow arterial and intramyocardial injection of ^{86}Kr and ^{133}Xe . *Acta physiol scand* (1966) Suppl No 272 p 5
- SCHÖLZ R H and DODGE H T. The use of single plane angiocardigrams for the calculation of left ventricular volume in man. *Amer Heart J* 73 (1968) 325
- SCHENK JR W G and DEDICHEN H. Electric measurement of blood flow. *Amer J Surg* 114 (1967) 111
- TENNANT R and WIGGERS C. The effect of coronary occlusion on myocardial contraction. *Amer J Physiol* 112 (1935) 331

LARGE VOLUME AORTOGRAPHY IN ATHEROSCLEROTIC PERIPHERAL VASCULAR DISEASE

A comparative investigation with conventional aortography

M. L. A. THOMAS and D. J. LINTOTT

The treatment most likely to benefit patients in atherosclerotic insufficiency to the lower limbs is surgical widening of stenotic or occluded segment of the arterial tree. Such operative therapy which may consist of grafting, vein bypass or endarterectomy depends on an accurate display of the arterial system to the legs. We believe that the most reliable and safe method of displaying the arteries in this disease is by translumbar aortography.

As these patients are frequently at high risk with generalized changes affecting particularly the coronary and cerebral arteries, any technique used should be as swift and accurate as possible.

Ideally the whole of the arterial system from the aorta to the ankles should be demonstrated using a single injection of contrast medium and one area of films. The difficulty in achieving this using a standard technique results from the variability in the number and severity of stenoses or occlusions and the presence of collaterals. This applies not only from patient to patient but also between one leg and the other in the same patient. These variables lead to

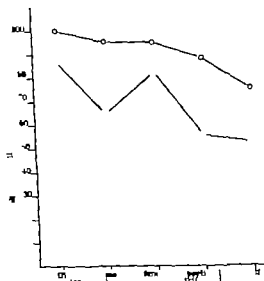


Fig 1 Results of large (o—o) and small (●—●) volume techniques

difficulty in timing of a series of films but this is much less critical when a large bolus of contrast is used

Little mention has been made in the literature of the volume of contrast medium which should be used in translumbar aortography but suggested amounts in the American and British literature vary from 15 to 20 ml (Goetz 1964 Surrow 1962 1969) although 40 ml or more are, as a rule used in the Scandinavian countries. In our experience the smaller quantities of contrast medium do not demonstrate the arterial tree sufficiently well to plan surgical treatment in many cases.

The object of this paper was to compare the results obtained using 80 ml of contrast medium (large volume) with those obtained using 20 ml (small volume).

Material Fifty consecutive patients with arterial insufficiency to the legs were investigated by translumbar aortography. Two injections were made at each examination the first using 20 ml of contrast medium the second using 80 ml. The two series of films were compared.

Method Because injection of contrast medium into atherosclerotic arteries is painful and the depth of tissue through which the needle must pass makes it difficult to obtain adequate local anaesthesia the examinations are carried out under general anaesthesia.

An AOT cut film changer with an automatic moving table top is used.

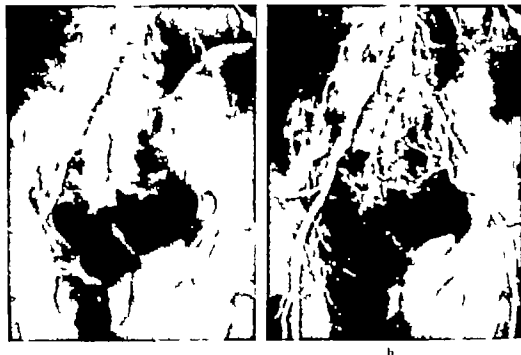


Fig. 1. a) Small of the left iliac and upper femoral arteries not demonstrated b) Large of the occluded segment of common iliac artery with patent external iliac and upper femoral arteries

With the patient in the prone position at St Thomas Hospital transumbilical aortography needle (LEA THOMAS & FLETCHER 1970) is introduced through the skin on the left side at a point midway between the 11th rib and the iliac crest one hand's breadth (including the thumb) from the midline. The needle is directed upwards and medially at an angle of about 20° and advanced until it hits a vertebral body. The needle is then withdrawn and readvanced more laterally until it passes the vertebral body and enters the aorta. Using this technique the aorta is usually punctured just below the renal arteries. The needle measures 15 cm in length is 16 gauge and has an occluded end with a side hole.

When a pulsatile blood flow is obtained from the needle a control 35 cm \times 35 cm film of the abdomen is exposed after a test injection of 5 ml of contrast medium to ensure that the side hole of the needle lies in the aortic lumen and that there is no stripping of the wall. If this preliminary film is satisfactory the main injection of 20 ml or 80 ml is injected using a pressure pump. The contrast medium used is sodium iothalamate 70% which combines a low



Fig 3 a) Small volume Left ilia and upper femoral arteries not demonstrated b) Large volume Full extent of occlusion demonstrated Upper femoral artery filling through collateral



Fig 4 a) Small volume Occlusion of both superficial femoral arteries indicated but extent not demonstrated. b) Large volume Full extent of occlusions well demonstrated



Fig. 1. (a) Small bubble popliteal artery occlusion demonstrated. (b) Image of same popliteal artery distal to block now filled.

viscosity with a high concentration. A series of films is exposed from the upper abdomen to the ankles. Three films are exposed in each of four positions, the first exposure being taken half way through the injection. The rate of exposure is usually one film per second but if on the test injection the aorta or both common iliac arteries are occluded or considerably dilated films are taken one every two seconds.

Using our needle, connector, contrast medium and pressure pump the injection rate is 10 ml per second.

Results

For the purpose of this investigation the arterial system of the legs was divided into the following regions: the aortic bifurcation, the iliac arteries (external and internal), the femoral arterial origins and femoral arteries (superficial and deep), the popliteal arteries (including the bifurcation) and the calf arteries as far as the ankles.

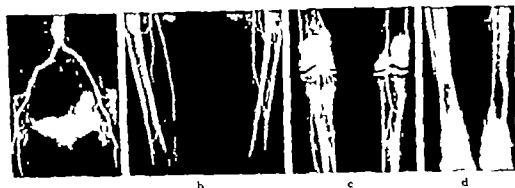


FIG. 6 Large volume translumbar aortogram. Arterial system from aorta to the arteries to ankle level filled.

All examinations using either small or large volumes of contrast medium demonstrated the aortic bifurcation adequately. The results in the remaining regions are shown in Fig. 1.

In the small volume examinations the iliac arteries were diagnostically filled in 87 per cent of legs, both femoral origins in 60 per cent, the femoral arteries in 32 per cent, the popliteal arteries in 36 per cent and the calf arteries in 52 per cent.

Using the large volume technique the iliac arteries were filled diagnostically in 100 per cent of legs (Figs 2, 3), the femoral origins in 90 per cent (Figs 2, 3), the femoral arteries in 94 per cent (Fig. 4), the popliteal arteries in 88 per cent (Fig. 5) and the calf arteries in 75 per cent (Fig. 6 d).

In only 35 per cent of legs examined using small volume was the whole arterial system down to and including the popliteal trifurcation adequately demonstrated. Using the large volume of contrast medium 83 per cent were diagnostic in all areas as far as the popliteal trifurcation (Fig. 6).

In every instance the large volume method demonstrated the arterial system more clearly and made interpretation of the films easier.

In 6 patients a significant lesion (i.e. occlusion or stenosis of a half or more of the lumen) was demonstrated only with the large volume (Fig. 7) and in 16 patients there were misleading appearances with the conventional dose suggesting the presence of a significant lesion which was shown not to be present with the high dose (Figs 2, 3, 4, 8).

Discussion

We have found translumbar aortography safer in patients with atherosclerotic disease of the aorta and its branches than femoral catheterisation which can lead to occlusion in narrowed and diseased arteries. Nevertheless, the conclusions



b

Fig 7 a) Small volume Popliteal artery faintly filled b) Large volume Tight stenosis of popliteal artery missed by small volume technique



a

b

Fig 8 a) Small volume Apparent occlusion of origin of superficial femoral artery b) Large volume Superficial femoral artery patent but irregular

drawn from this paper would apply to both techniques. Similarly, although we have found an AOT film changer with moving table top most convenient the same principles apply whatever angiographic equipment is used.

No complications due to either the translumbar technique or to the contrast medium have been encountered in this series.

The total volume of contrast medium used was about 100 ml in each patient. It must be admitted that the use of a large volume must increase the concentration of contrast medium entering the visceral and spinal arteries. With our technique the needle puncture was made below the renal arteries and none of our patients had a total aortic occlusion. Most of the serious complications, such as renal failure (ABRAMS 1957, 1961; ANSELL 1968; GRAINGER 1965; McAFEE 1957) and paraplegia (DJINDJIAN & FAURE 1967; HARE 1957) occurred with the old contrast media (acetrizoate and diiodone) and few complications of this nature have been reported using the modern media (GRAINGER). Against this slight risk of complications from the increased volume of contrast medium must be set the advantages of a single injection resulting in an adequate examination in the shortest possible time. Such an examination with a single injection and series of films takes only about half an hour from the induction of the anaesthetic to the completion of the examination.

A large bolus of contrast medium not only demonstrates the arterial system and any lesions present more clearly but also makes the timing of the series of films less critical.

Although the proximal end of an arterial occlusion may be demonstrated with the small volume (Figs 2 a 3 a, 4 a) the distal end is often only demonstrated with the large volume examination (Figs 2 b 3 b 4b) This is important when planning surgical treatment

Also using a large volume of contrast medium it is less likely that significant lesions will be missed and the possibility of obtaining misleading films will be avoided

We therefore conclude that large volume translumbar aortography is more accurate and produces fewer misleading appearances than the technique most often employed

SUMMARY

Fifty consecutive patients with arterial insufficiency of the lower limbs were investigated by large volume translumbar aortography using 80 ml of sodium iothalamate 70%. The results were compared with an examination in the same patient using 20 ml of the same medium. In the small volume technique only 35% of the examinations were judged of diagnostic quality in all areas down to and including the popliteal trifurcation whereas in the 80 ml technique 83% were diagnostic. As no complications were encountered it is suggested that large volume translumbar aortography is the method of choice for the investigation of atherosclerosis of the lower limbs.

ZUSAMMENFASSUNG

Fünfzig nacheinanderfolgende Patienten mit arterieller Insuffizienz der unteren Glieder wurden mit translumbarer Grossvolumen Aortographie unter Anwendung von 80 ml 70 % igeu Natrium Iothalamat untersucht. Die Ergebnisse wurden mit Untersuchungen an selben Patienten unter Anwendung von 20 ml desselben Mittels verglichen. Bei der Technik mit dem kleinen Volumen wurden nur 35 % der Untersuchungen von diagnostischer Qualität in allen Abschnitten herab bis einschließlich der Trifurkation der Poplitea befunden, während bei der 80 ml Technik 83 % diagnostisch Qualität aufwiesen. Da keine Komplikationen auftraten, wird die translumbare Grossvolumen Aortographie als Methode der Wahl bei Untersuchungen der Arteriosklerose der unteren Extremitäten vorgeschlagen.

RÉSUMÉ

Cinquant malades consécutifs atteints d'insuffisance artérielle des membres inférieurs ont subi une aortographie par oc lombaire avec une grande quantité de moyen de contraste 80 ml d'iothalamat de sodium 70 %. Les résultats ont été comparés ceux d'un examen du même malade avec 20 ml du même moyen de contraste. Avec la technique utilisant une petite quantité de moyen de contraste 35 % seulement des examens avaient une bonne qualité diagnostique dans toutes les régions jusqu'et y compris la trifurcation

populée alors que 83 des examens faits à ce 80 ml donnaient le diagnostic. Étant donné qu'il n'y a pas eu de complication les auteurs pensent que l'aortographie par voie lombaire avec une grande quantité de moyen de contraste est la méthode de choix pour l'examen de l'athérosclérose des membres inférieurs.

REFERENCES

- ABRAMS H. L. Radiologic aspects of operable heart disease: hazards of retrograde thoracic aortography. *Radiology* 68 (1977) 81.
 — Aortography. Vol. 1, p. 163. Little Brown & Co. Boston 1961.
 AVALL G. National survey of radiological complications: interim report. *Clin Radiol* 19 (1968) 175.
 DYNDJI R. and FALKE C. Spinal cord complications of aortography. *J. belge Radiol* 50 (1967) 207.
 GOETZ R. H. Vascular roentgenology, p. 344. Edited by R. A. Schobinger and F. E. Runck. Macmillan Co. New York 1964.
 GRAINGER R. G. Complications of cardiovascular radiological investigations. *Brit. J. Radiol* 38 (1965) 201.
 HARR W. Damage to spinal cord during translumbar aortography. *J. Fac. Radiol* 8 (1955) 258.
 LEA THOMAS M. and FLETCHER E. W. L. Large volume translumbar aortography in aortic occlusion. *Amer. J. Roentgenol* 109 (1970) 541.
 McVIE J. G. Survey of complications of abdominal aortography. *Radiology* 68 (1957) 835.
 SUTTON D. Arteriography, p. 103. Livingstone Ltd. Edinburgh and London 1966.
 — A text book of radiology, p. 569. Edited by D. Sutton and R. G. Grainger. Livingstone Ltd. Edinburgh and London 1967.

ANGIOGRAPHIC APPEARANCES OF AN INTRAMUSCULAR HAEMATOMA

M. LEA THOMAS and M. R. ADDRESS

The diagnosis of soft tissue masses in the extremities may be difficult on clinical grounds alone and for this reason angiography is often undertaken (MAROULIS & MURPHY 1958; ROSENBERG 1964). One of the less usual conditions is a spontaneous muscle rupture with haematoma formation. There have been few descriptions of the angiographic appearances in this condition and we report this case to draw attention to these appearances and to describe an unusual finding not previously reported which made it difficult to differentiate the lesion from a malignant tumour.

Case report

A woman aged 64 was admitted with one year history of episodes of pain and swelling in the right knee followed on two occasions by swelling and bruising in the calf. There was no history of trauma. On examination there was an effusion in the knee joint. A firm rounded mass was palpable deeply in the upper medial part of the calf. It was considered that the two episodes of swelling and discolouration in the calf were due to haemorrhage possibly from an arteriovenous malformation or tumour. The patient had normal bleeding and coagulation times.

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Fig. 1 Arterial plaque.
 Displacement of arterial
 lumen by irregular mass
 the posterolateral part of
 the popliteal and beaded
 irregularity \rightarrow of adjacent
 arteries.



Fig. 2 Late phase. Rim
 of contrast medium
 surrounding lesion and popliteal
 filling of popliteal vein
 while contrast medium is
 still present in the small
 arteries.



Femoral angiography showed the presence of an old mass situated deep to the medial head of gastrocnemius muscle. Normal sized sural branches of the popliteal artery were displaced around the mass and more peripherally the supplying arteries had an irregular beaded appearance (Fig. 1). There was rapid passage of contrast medium into the popliteal vein (Fig. 2). While contrast medium was still present in small arteries. In the early venous phase a dense rim of contrast filled vessels surrounding the lesion were shown (Fig. 3). No pathologic vessels could be identified.

At operation the mass was shown to be an organising haematoma with granulation tissue around its margin. No cause was found.

Discussion

Malignant tumours of the soft tissues of the extremities can be diagnosed with a high degree of accuracy in the presence of definite pathologic vessel. Difficulties arise where the abnormality demonstrated consists of increased vascularity alone. Such a lesion is more likely to be either a benign tumour or an inflammatory process. However since some malignant tumours do not have pathologic circulation angiography cannot exclude such a lesion. In such instances the clinical findings may be the deciding factor in treatment.

Our patient fell into the above category. The age of the patient, the history of recurrent episodes of swelling and bruising and the absence of trauma did not suggest a diagnosis of muscle rupture and an arteriovenous malformation or tumour with episodes of haemorrhage seemed more likely.

The angiographic appearances of increased vascularity particularly around the circumference of a deeply situated mass with early arteriovenous shunting and no definite pathologic circulation favoured an inflammatory lesion such as an organising haematoma (STENER & WICKBOM 1966). However in addition to these characteristic findings supplying arterial branches had an irregular lumen, a feature not previously described in this condition. The appearances of this irregularity was similar to those sometimes seen elsewhere when malignant processes such as carcinomas of the pancreas and meningiomas involve adjacent arteries. Because of this feature and the fact that tumours do not necessarily have a pathologic circulation (COCKSHOTT & EVANS 1964) operative removal was considered advisable.

The angiographic appearances of an organising haematoma are essentially similar to those seen in other chronic inflammatory processes (STENER & WICKBOM). The collection of contrast medium around such lesions and the arteriovenous shunting are presumed to be due to contrast passing through the abundant capillaries in the granulation tissue (LAGERGREN *et al.* 1958; MARGULIS & MURPHY 1958). The pathologic basis for the irregularity of the arteries in our case may perhaps be explained by deformity due to contraction with maturation of granulation tissue in the organising haematoma.

SUMMARY

The angiographic appearances of an intramuscular haematoma resulting from spontaneous calf muscle rupture are described. These consisted essentially of collection of contrast medium around the periphery of a circumscribed mass with arteriovenous shunting. Beaded irregularity of supplying arterial branches was also observed, a feature not previously described in this condition but similar to that sometimes seen in malignant processes.

ZUSAMMENFASSUNG

Das angiographische Bild eines intramuskulären Hämatoms als Folge einer spontanen Wadenmuskulaturruptur wird beschrieben. Dieses bestand vorwiegend aus einer Ansammlung von Kontrastmittel um die Peripherie einer umschriebenen Masse mit einem arteriovenösen Blutshunt. Eine peripher marginale Unregelmäßigkeit der ernährenden arteriellen Zweige wurde ebenfalls beobachtet, ein Bild, das zuvor nicht unter dieser Bedingung beobachtet worden ist, aber ähnlich dem Zustand ist, der gelegentlich bei malignen Prozessen zu sehen ist.

RÉSUMÉ

Les auteurs décrivent les aspects angiographiques d'un hématome intra musculaire consécutif à une rupture spontanée des muscles du mollet. Ces signes consistent essentiellement en une accumulation de moyen de contraste autour d'une masse circonscrite contenant des communications artério-veineuses. Ils ont aussi observé des irrégularités moniformes des branches artérielles afférentes signe qui n'avait pas été décrit dans cette affection mais qui (semblable) à modifications artérielles qui existent parfois dans des tumeurs malignes.

REFERENCES

- COCCHIOTTI W. P. and E. ANDERSON T. The place of soft tissue arteriography. *Brit. J. Radiol.* 37 (1964) 367.
- LAGERGREN C., LINDBOM Å. and SÖDERBERG G. Hypervascularisation in chronic inflammation demonstrated by angiography. *Acta radiol.* 49 (1959) 441.
- M. ROLLS A. R. and M. R. ANDRESS T. O. Arteriography in neoplasms of extremities. *Amer. J. Roentgenol.* 80 (1958) 330.
- ROSENBERG J. C. The value of arteriography in the treatment of soft tissue tumours of the extremities. *J. Int. Coll. Surg.* 41 (1964) 403.
- STENER B. and WICANDER I. Angiography in three cases of muscle rupture with organised haematoma. *Acta radiol. Diagnostica* 4 (1966) 169.

INFLUENCE OF NEPHROANGIOGRAPHY ON ¹²⁵I HIPPURAN NEPHROGRAPHY

J HAUDE and I NORDENFELT

MALAMOS et coll (1968) investigated the influence of translumbar aortography on radioisotope nephrography and reported that the procedure affected the latter in 31.5 per cent of cases during the first week of the post angiographic period. The authors therefore recommended that the isotope examination should be performed no sooner than 7 days after aortography. They examined 25 patients, mainly with hypertension by translumbar aortography under general anesthesia with Urografin 76 % as contrast medium injected by hand. This technique is nowadays seldom used. The investigation gave no information on the influence of selective nephroangiography on isotope nephrography. Therefore it appeared justified to investigate such influence in a series of cases examined by selective angiography. It was also thought possible to determine if the function of a kidney already damaged by disease was more liable to be affected by angiography than that of a normal kidney.

Material and Methods Forty nine patients from 19 to 73 years of age were included. One patient was examined twice. A total of fifty angiographies and isotope nephroographies in 100 kidneys before and after angiography were performed.

Table 1

1 giv. of the diagnosis 49 patients 50 examinations except gated by pre and post angiographic and per nephrography

Diagn.	N. of examinations performed	N. of patients with changes in post angiographic isotope nephrograms
Renal artery stenosis	5	1
Renal vein thrombosis	1	—
Renal pelvis	—	—
Renal calculi and renal cysts	1	1
Chronic pyelonephritis	10	2
Chronic pyelonephritis and renal artery stenosis	1	—
Bilateral nephrosis	6	—
Renal pelvis	—	—
Chronic glomerulonephritis	1	—
Nephroses	2	—
Renal infarct	1	—
Congenital hypoplasia	1	1
Normal angiography	10	1
Total	50	6

One patient examined twice

Angiography normal Calculus in the renal pelvis

Isotope nephrography The pre angiographic isotope nephrography was performed usually within 2 to 3 weeks before the angiography. Where the interval between the nephrography and the angiography was longer the renal condition was considered to be stationary and not to be the cause of a change in the post angiographic nephrogram. The isotope examination was performed 6 hours to 5 days after the angiography. Eight isotope examinations were performed on the same day as the angiography and on the first, second and third day following it. Eleven were carried out 4 days and seven 5 days after the angiography. Control examinations were performed on recovery.

Isotope nephrography was performed with scintillation detectors (50 mm × 50 mm) ratemeters combined with single channel analysers (Wallac, Finland) and lead collimators with rectangular apertures (vertical width 94 mm horizontal width 47 mm). The collimators were sited touching the skin and the detectors were recessed from the surface (skin-crystal distance 150 mm). The position of the kidneys was determined with a hand scintillation detector after intravenous injection of 10 mCi ^{99m}Tc Hippuran (sodium ortho iodo-hippurate). The patients

Table 2

Number of patients and impaired kidneys at isotope nephrography 0 to 4 days after nephroangiography compared to the results of isotope nephrography before angiography

No. kidney	Zero		One		Two		Three		Four		Five		Total
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	
Results													
Unchanged	6	7	7	8	8		7	7	11	10	7	7	92
Impaired		1	1	0	0	1	1	1	0	1	0	0	8

had been well hydrated by drinking 1 000 ml of water starting 60 minutes and ending 30 minutes before the beginning of the test. This water load resulted in diuresis with a total urine flow of 6.2 ± 4.0 (SD) ml/min. an intravenous dose of 10 mCi of ^{131}I Hippuran was administered. The isotope nephrograms were recorded on a two-pen recorder (Honeywell Elektronik 194) at a chart speed of 1.25 cm/min and a time constant of 4 s. the patients were examined sitting.

Angiography. All examinations were performed with percutaneous catheterization of the femoral artery. Bilateral elective nephroangiography was carried out in 17 patients, while only one kidney was examined in 3 patients. Both lumbar aortography and bilateral elective angiography were performed in 14 patients. Twelve patients were examined with a bilateral semi-elective catheterization technique, i.e. the tip of the catheter was placed into one of the renal arteries while the sideholes positioned in the aorta directed the flow of contrast medium into the contralateral kidney. 4 patients received only an aortic injection.

A latex thin walled catheter (OD 2.2 mm ID 1.45 mm) was used. for the semi-elective technique and aortography the tip was pulled out 2.5 cm and the distal part of the stem of the catheter was provided with 6 sideholes. Usually two injections each of 6 to 10 ml Lopaque Cerebral (meglumine calcium salt of metrizoic acid containing 280 mg I/ml Nyegaard Oslo) were given for elective nephroangiography at about 10 ml/s for semi-elective nephroangiography and aortography 24 to 30 ml contrast medium at a rate of 15 to 20 ml/s was the rule. The total amount of contrast medium including that for test injections varied between 24 and 280 ml per patient.

Results

The angiographic findings appear in Table 1. If possible the diagnosis was verified histologically. The diagnosis of cysts was confirmed by percutaneous renal puncture.

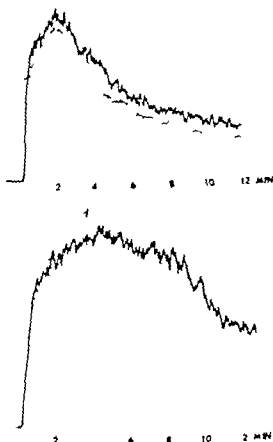


Fig. 1 Case 1 a) (top) Normal isotope nephrogram 55 days before angiography b) (bottom) Isotope nephrogram 6 hours after angiography. Right nephrogram (—) Slowing of the uptake and excretory phases. Left nephrogram (---) Essentially normal.

The post angiographic isotope nephrography in 6 patients (8 kidneys, Tables 1-2) presented changes that could be attributed to the angiography. The findings will be presented in detail and be the subjects of comment (Cases 1 to 6). The main alteration where changes in the post angiographic nephrograms were present was always slowing of the third (excretory) phase (Figs 1 b, 2 b, 3 b and 5 b) and sometimes small irregularities in this phase as well (Figs 1 b, 2 b). The second (uptake) phase was affected in 2 patients (Figs 1 b, 5 b). The pathologic changes in the isotope nephrograms could not be explained by differences in the total urine flow at the two examinations.

Case reports

Case 1 Female, aged 43. Pre angiographic diagnosis: Pyelonephritis, right kidney. Isotope examination 55 days before angiography was normal for both kidneys (Fig. 1 a). Angiography demonstrated a moderately scarred pyelonephritic right kidney. Isotope nephrography

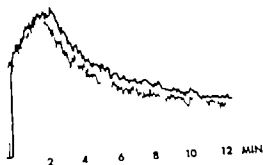


Fig. 1 a) (top) Normal isotope nephrogram one day before angiography b) (bottom) Isotope nephrogram 6 hours after angiography Right (—) and left (---) nephrograms. Slowing of the excretory phase more marked on the right side

6 hours after angiography was essentially normal for the left kidney, on the right side it revealed slower uptake phase than at the pre-angiographic examination and slow slightly irregular excretory phase (Fig. 1 b). The abnormalities disappeared two days later.

Comment. A total of 90 ml contrast medium was injected. Five injections each of 8 ml were made selectively into the right renal artery (examinations were repeated because of technical hitch at filming). Only 8 ml were injected selectively into the left renal artery and 30 ml used for the aortography. Twenty ml were injected as test. No complications occurred at angiography. The diseased right kidney thus received a much larger amount of contrast medium than the normal left kidney and thus possibly caused the reversible changes in the post-angiographic isotope nephrography.

Case. Male aged 59. Pre-operative evaluation because of a calculus in the left renal pelvis. Isotope nephrography (Fig. 2 a) one day before a normal angiography revealed no abnormality. Nephrography performed 6 hours after angiography demonstrated slight slowing of the left and more marked slowing of the right excretory phase (Fig. 2 b).

Comment. Two injections each of 10 ml contrast medium were made into both renal arteries for the selective examination. Aortography was performed with 40 ml contrast

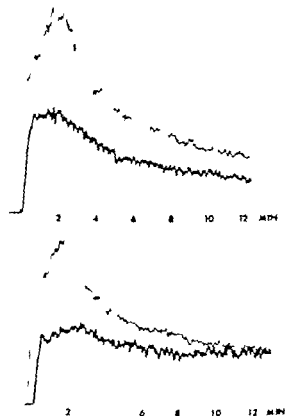


Fig. 3 (a, b). (a) (top) Isotope nephrogram of the right kidney before angiography. (b) (bottom) Isotope nephrogram one day after angiography. Right nephrogram (—) (---) maximum and sloping of the excretory phase. Left nephrogram (—) (---) normal.

medium and less than 10 ml were used for tests. Following angiography the arterial catheter was left in situ and both renal arteries were selectively catheterized for renal flow measurements with the dilution technique (Gottman & Olsson 1970). During this procedure a hematoma developed at the site of puncture. The blood flow in both kidneys was markedly reduced (190 ml/min right and 235 ml/min left; normal values 400–500 ml/min). This bilateral reduction of kidney perfusion was most likely caused by the fall in blood pressure from 140 to 100 mm Hg systolic during the examination and probably contributed to the abnormal post-angiographic isotope nephrography. Two days later the isotope examination was normal.

Case 3. Female, aged 22. Pre-angiographic diagnosis: Chronic pyelonephritis. The left isotope nephrography before the angiography was normal and the right curve indicated reduced function of the kidney (Fig. 3). Later the same day bilateral selective nephroangiography demonstrated pyelonephritis of both kidneys. The changes were more marked in the small contracted (9.5 cm \times 5.5 cm) right kidney (Fig. 4). Isotope examination one day after the angiography disclosed unchanged and normal appearances on the left side but on the right side the maximum was reached later and the excretory phase had become slower (Fig. 3 b).

Comment. A total of 80 ml contrast medium was injected (25 ml semiselectively into both renal arteries, 30 ml were used as test). With the difference in the size of the kidneys the small contracted right kidney received relatively more contrast medium than the left

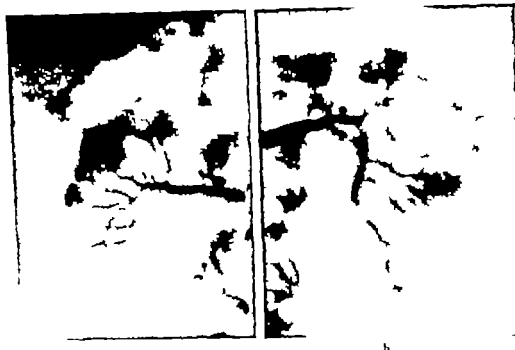


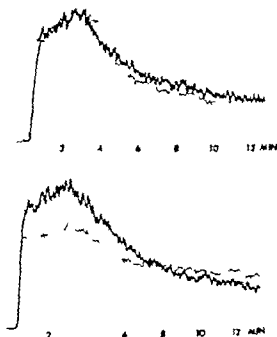
Fig. 4. Ca. 3. Bilateral semi-lectin nephroangiography. a) Contracted pelonephritic right kidney. b) Reduced parenchyma at upper pole of left kidney.

kidney and thus possibly influenced the function of the already severely pelonephritic right kidney. Repeat isotope nephrography 2 months after angiography still indicated a slow excretory phase on the right side. Seven months later the nephrographic findings were restored to the level before the angiographic examination.

Case 4. Male, aged 22, examined for proteremia. One day before angiography the isotope nephrography was normal (Fig. 5). Angiography revealed that the left kidney was supplied by two arteries. No morphologic changes in the kidney were present. Two days after angiography the left isotope nephrogram disclosed slow uptake and excretory phases (Fig. 5b). The right nephrogram was unchanged and normal.

Comment. A total of 80 ml contrast medium was injected. 40 ml were used for test injections and 2 injections each of 10 ml were made selectively into the right renal artery. Selective catheterization of both arteries to the left kidney produced marked spasm, resulting in reduced renal flow (Fig. 6). Two injections each of 8 ml of contrast medium were made into the dorsal renal artery and 9 ml were injected into the ventral renal artery. The abnormal left post-angiographic isotope nephrogram was most likely the result of ischemia, thus was probably caused by reduced blood flow secondary to arterial spasm at selective catheterization, accentuated by relatively large amounts of contrast medium injected into both renal arteries and not washed out because of reduced perfusion of the kidney. Unfortunately, the isotope examination was not repeated and it is not known if the function of the left kidney recovered.

Fig. 5 Case 4 a) (top) Normal isotope nephrogram one day before angiography b) (bottom) Isotope nephrogram 2 days after angiography Right nephrogram (—) Normal Left nephrogram (---) Slowing of the peak and excretory phases



Case 5 Female aged 65. Angiography was indicated by hypertension and a tumour in the right kidney observed at urography. The isotope nephrography four days before angiography was normal. Bilateral selective nephroangiography revealed carcinoma of the right and multiple cysts in the left kidney. Three days after the angiography isotope nephrograph disclosed slow and irregular excretory phases on both sides; these changes had not disappeared four days later.

Comment. Selective nephroangiography was performed with 2 injections into both renal arteries (each injection of 10 ml). 40 ml were used for test. No angiographic complications occurred. The cause for the changes in the post angiographic isotope nephrography is not obvious. It is remarkable that the changes persisted seven days following the angiography.

Case 6 Male aged 55 examined for hypertension. Isotope nephrograms on both sides one day before angiography were normal. Angiography revealed moderate hypoplasia of the left kidney. Isotope nephrography four days later indicated a slower excretory phase of the left kidney than before; the right remained normal. Six days after the angiography the left isotope nephrogram disclosed improved conditions which had however not returned to normal at a repeat control 25 days after angiography.

Comment. Both kidneys were examined by both semiselective and selective techniques. Thirty ml contrast medium were used for the semiselective examination, 10 ml being injected selectively into the right and the same amount twice into the left renal artery. Because of a difficult catheterization 80 ml contrast medium were used for test injections. The total amount injected was thus 170 ml. No complications occurred at angiography and no definite

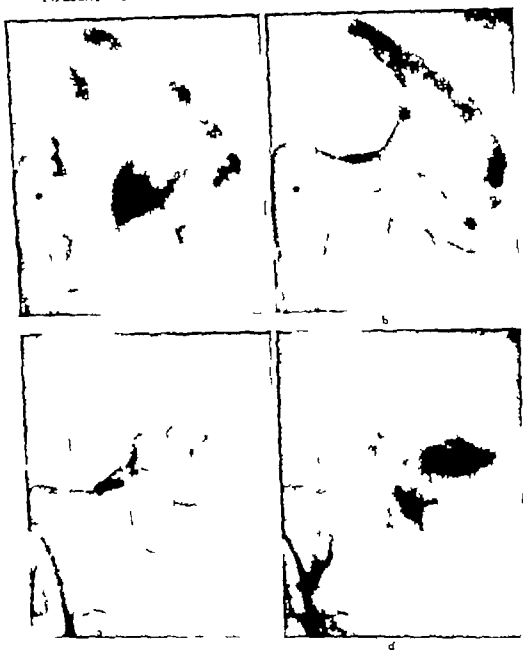


FIG. 6. Case 4. a) b) Selective angiography of the ventral artery of left kidney. Spasm of the catheterized artery causing severe reduction in renal perfusion. c) Beginning of the injection. Contrast medium in the kidney from the last injection performed shortly before serial filming. d) Four seconds following injection. Contrast medium still in the arteries. e) d) Selective angiography of the dorsal artery of the left kidney. Arterial spasm at tip of catheter causing reduced perfusion in parts of the kidney supplied by the dorsal artery.

explanation for the abnormal isotope nephrogram with persistent changes almost one month after the angiography can be offered. It is possible that the relatively large total amount of contrast medium affected the hypoplastic left kidney and caused the slowing of the excretory phase observed in the post-angiographic isotope nephrogram.

Discussion

Selective nephroangiography in experimental investigations produced slightly altered renal function immediately and 24 to 48 hours after angiography evident in the isotope nephrography (TAKARO 1967). The changes were observed after the selective injection of 0.2 to 0.4 ml/kg sodium iothalamate 66.8% into renal arteries in dogs.

Clearance tests are more quantitative examination methods of renal function than isotope nephrography and have been used to determine angiographic renal damage in animal by several authors (see HIRLANDER 1958). BOWER *et coll.* (1966) investigated the influence of the aortic injection of diatrizoate on the kidney by determination of inulin and PAH-clearance under mannitol diuresis and observed no significant alterations in renal function. However one patient had signs of vasoconstriction at 24 hours, these had disappeared at 10 weeks. SORBY & HON (1968) observed in 10 out of 12 patients a decrease of the PAH extraction ratio immediately following the initial aortic injection of diatrizoate, all but 2 had partial recovery within 20 minutes. They found no correlation between the degree of depression and the number of injections, the presence or absence of hypertension or elevated blood urea.

The contrast medium (Iopaque Cerebral) used in the present investigation is not known to be more nephrotoxic than diatrizoate or iothalamate agents.

Changes in the isotope nephrogram caused by nephroangiography might be attributed to one or a combination of the following factors: saturation of the tubular transport mechanisms by the contrast medium, reduction of the perfusion of the kidney, or toxic and ischemic damage to the tubular cells.

The main alterations in the post-angiographic isotope nephrogram were slowing or irregularities of the excretory phase. The changes are usually connected with disturbances in the outflow of urine and are the main findings in obstruction of the ureter. Angiography, however, does not affect the outflow tract of the kidney. It has also been claimed (FARMELANT *et coll.* 1964; BRITTON *et coll.* 1967; SACHS 1967) that reduced blood flow through the kidney will cause slowing of the excretory phase. The uptake phase was affected in 2 of the present patients. This phase is known to be dependent on the perfusion of the kidney and the function of the tubular cells.

Four abnormal isotope nephrograms in 32 kidneys examined (12.5 per cent) were obtained during the first 24 hours following angiography, two to five days

after angiography 4 out of 68 i.e. only 6 per cent, were abnormal. This indicates that any possible angiographic damage to the kidney function is usually reversible within a few days.

Saturation of the tubular transport mechanisms will cause flattening of the uptake and excretory phases of isotope nephrography performed shortly after urography (TARLIN 1966). This might be the explanation of the changes in Cases 1 and 2 in which the isotope nephrography was carried out 6 hours after the angiography. Another possible explanation exists however in Case 2 i.e. reduction in the perfusion of the kidneys probably due to fall in the blood pressure. Nevertheless, saturation of the tubular cells with contrast medium cannot be a common cause of changes in the isotope nephrography performed within 6 hours after angiography as only 3 out of 16 nephrograms were affected.

Reduction in the kidney perfusion is probably the main cause of changes in post angiographic isotope nephrography. If the perfusion be markedly reduced it may lead to ischemic or toxic damage of the tubular cells as the contrast medium will not be washed out as rapidly as it should be. Reduced perfusion of the kidneys may be caused either by a fall in blood pressure as probably happened in Case 2 or by spasm of the renal arteries secondary to catheterization which was observed during the angiography in Case 4. In the latter a delayed washout of contrast medium was also evident and additionally relatively large amounts were used for selective injection. Experimental investigations have also indicated that spasm of the renal artery induced by elective catheterization results in reduced renal circulation (LINDELL & OLIN 1957; HELANDER 1958).

It is thus reasonable to assume that the changes in the post angiographic isotope nephrograms in Cases 2 and 4 were caused by reduced blood flow to the kidneys resulting in ischemic or toxic damage of the tubular epithelium. It may be however that loading of the tubular cells with contrast medium in Case 2 contributed to the changes in the isotope nephrography. The assumption that the kidney perfusion was reduced by a fall in blood pressure during the examination from 140 to 100 mm Hg systolic is supported by the fact that in no other patient was such a difference in blood pressure before and after angiography recorded.

No apparent cause of the abnormal post angiographic isotope nephrogram was apparent in Cases 5 and 6. The hypoplastic left kidney in Case 6 received however a large amount of contrast medium causing possible toxic damage of the tubular cells. The changes in the nephrograms in the 2 cases still persisted at control examinations at 7 and 25 days respectively after angiography indicating that they were not easily reversible.

A contributory factor to abnormalities in the post angiographic isotope nephrogram may be that the kidneys were diseased (or hypoplastic) which is also applicable to Cases 1 and 3. The number of diseased kidneys with abnormal

post angiographic isotope nephrography was 5 out of 41 while out of 59 normal kidneys only 3 such examinations were abnormal (Cases 2 and 4) and most likely because of complications at the angiography causing reduced kidney perfusion. The present investigation thus also indicates that it is possible that in the presence of pre-existing renal diseases — whatever its nature — an isographic damage of kidney function is more likely to occur than in healthy kidneys. Isotope nephrography failed in 2 patients to indicate that this damage was reversible. No clinical progress of the disease or impairment of renal function was however noted.

Conclusion

Nephroangiography may cause impaired kidney function as revealed by isotope nephrography. The damage is usually reversible. These changes are probably caused in healthy kidneys by reduced renal perfusion secondary to a complication at angiography such as arterial pain or fall in blood pressure. Changes in the post angiographic isotope nephrography in pre-existing renal disease may also occur without any complication at angiography. The results of the present investigation stress the importance of a careful technique for the selective catheterization of renal arteries. Selective catheterization of small accessory arteries should be avoided if not absolutely necessary (for example to exclude small or partially vascularized neoplasia).

The incidence of abnormalities in post angiographic isotope nephrograms is much less than that reported by MALAMOV *et coll.* (8 per cent in the present, 31.5 per cent in the work of MALAMOV). However they do occur and isotope nephrography should be carried out before angiography. An abnormal post angiographic isotope examination should be repeated because the changes may have been caused by the angiography and recovery can be expected.

SUMMARY

The influence of nephroangiography on isotope nephrography was investigated in 41 patients. The post angiographic isotope nephrogram was abnormal in 8 per cent of the kidneys examined. Complications at angiography such as spasm of the renal artery or fall in blood pressure affect the perfusion of the kidney and may lead to an abnormal isotope nephrogram. Renal function appears to be more vulnerable to angiography in a diseased than in a healthy kidney.

ZUSAMMENFASSUNG

Der Einfluss der Nephroangiographie auf die Isotopen Nephrographie wurde bei 49 Patienten untersucht. Die post angiographisch Isotopen Nephrographie war in 8 Prozent der untersuchten Nieren pathologisch. Komplikationen bei der Angiographie wie Spasmen

der Nierenarterie oder Blutdruckfall beeinflussen die Perfusion der Niere und können somit zu einem pathologischen Isotopen Nephrogramm führen. Die Nierenfunktion scheint bei einer kranken Niere gegenüber der Angiographie empfindlicher als bei einer gesunden Niere zu sein.

RÉSUMÉ

Les auteurs ont étudié l'influence de la néphroangiographie sur la néphrographie isotopique chez 49 sujets. La néphrographie isotopique post angiographique a été anormale sur 8 pour cent des reins examinés. Les complications de l'angiographie tels que les spasmes de l'artère rénale ou les chutes de pression artérielle affectent la perfusion du rein et par conséquent le résultat de l'examen. L'angiographie perturbe plus la fonction rénale des reins malades que celle des reins sains.

REFERENCES

- BOWER J. D., NAGRE J. H. and LESTER R. G. The effect of renal angiography on the normal kidney. *Surgery* 60 (1966) 545.
- BRITTON K. E., BROWN N. J. G. and SLATER J. D. H. Isotope renography. *Lancet* 1969 I p. 986.
- FARNSWORTH M. H., SACHS C. H., GENNA S. and BURROWS B. A. Physiological basis of radioisotopic renal function studies. *Clin. Res.* 12 (1964) 251.
- GOTTLIN J. och OLIN T. Nefroangiografi kompletterad med blodflödesmätning enligt färgspåringsmetoden. (In Swedish). *Nord. Med.* 84 (1970) 1317.
- HELANDER C. G. Nephrographic effect and renal arteriographic damage. An experimental study. *Acta radiol.* (1958) Suppl. N. 163.
- LYNDALL S. E. and OLIN T. Catheterization of the renal arteries in dogs and cats. *Acta phys. scand.* 39 (1957) 73.
- KLAMANN B., CHRISTEAS N., GYFRALI E. et coll. The influence of angiography on the radioisotope renogram. *Nord. Med. (Stockh.)* 7 (1968) 222.
- SACHS C. H. Bases physiologiques du néphrogramme isotopique au radiohippuran. *Actualités néphrol. Hop. Necker* (1967) 283.
- SORRY W. A. and HOY R. J. Renal arteriography and renal function. The short term effect of angiography selectively renal arteriography, adrenal suppression and renal angiography on PAH extraction ratio. *Amst. Radiol.* 12 (1968) 52.
- TAKARO T. Experimental renal glomerulography. *Amer. J. Roentgenol.* 101 (1967) 681.
- TAPLIN G. V. Radioisotope renography in renovascular hypertension. *Postgrad. Med.* 40 (1966) 302.

PHLEBOGRAPHIC SIGNS IN EARLY POSTOPERATIVE VENOUS THROMBOSIS OF THE LOWER EXTREMITY

B E ZACARIUSSEN and H J JANSEN

The clinical diagnosis of venous thrombosis is often difficult and different opinions exist concerning the phlebographic criteria of the early stage. COON & COLLIER (1959) reported that a clinical diagnosis of venous thrombosis had been made in only 10.6 per cent of 595 cases of pulmonary emboli evident post mortem. HÄGER (1965) stated that in half of the cases the diagnosis is usually wrong and based his opinion on 512 cases in which it had previously been made on clinical grounds but in 46 per cent of which phlebography had revealed normal veins. MAY & NISSEL (1967) reported incorrect diagnoses in about 25 to 30 per cent of early cases.

BECKER *et coll* (1970) have recently reported silent deep vein thrombosis following prostatectomy in 26 of 166 cases (16 per cent). BOMSTROM *et coll* (1963) were the first to make this observation in patients surviving with trochanteric fractures. Similar results of silent postoperative thrombosis have been reported by NEZOS *et coll* (1968) and FLANC *et coll* (1969) with ¹²⁵I labelled fibrinogen.

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Table 1

Age and sex distribution of 68 cases of postoperative venous thrombosis

	30-39	40-49	50-59	60-69	70-79	80-89	90	100	Total
Men	1		7	18	10	3	1		40
Women			7	10	11				28
Total	1		14	28	21	3	1		68

All this suggested that the clinician required confirmation of the diagnosis of venous thrombosis. FRIMANN DAHL (1935) pointed out that the diagnosis could be made roentgenologically by phlebography, an opinion supported by the investigations of DOS SANTOS (1938), BAUER (1940) and LINDBLOM (1941) and later by GREITZ (1954-1955), GULLNO (1956), ALMER & NYLANDER (1962-1964), DE WEESE & ROOFOFF (1963), BOROSTROM *et coll.* MAY & NISSE, HJELMSTEDT & BERGVAL (1968), NYLANDER (1968), BECKER *et coll.* BERGVAL (1971) and others. Both LINDBLOM and GREITZ emphasized that phlebography should be carried out with the extremity in a vertical rather than a horizontal position to eliminate the sources of errors caused by layering of the contrast medium.

Different criteria appear in the literature regarding the phlebographic diagnosis of fresh venous thrombosis. The nomenclature also varies and in addition to fresh early and recent thrombosis the term acute thrombosis is often used. Most investigators consider constant filling defect in a vein to be a sign of fresh (acute) thrombosis (HELLSTEN 1942), DE WEESE & ROOFOFF, BOROSTROM *et coll.* MAY & NISSE, LEA THOMAS 1970, BERGVAL and others). Some writers claim that non filling of the deep veins in the lower leg combined with increased velocity of flow in the superficial veins is a significant finding in acute cases (NYLANDER) while others doubt the reliability of such signs (BOROSTROM *et coll.* DE WEESE & ROOFOFF).

A review of the roentgenologic criteria of venous thrombosis described in the literature gives the following groups: (A) Constant filling defects: (1) floating thrombus (cylindrical defect in a contrast filled vein), (2) visible cupola of thrombus, (3) partially adherent thrombus (partial filling of deep veins with filling defects). (B) Non filling of deep veins: (1) total (only superficial veins filled rapid flow), (2) local deep vein obstruction, no thrombus, (3) local and combined with collaterals.

Group A is thus formed of direct positive diagnostic criteria as a thrombus or a part of a thrombus must be evident. Various indirect signs that could be

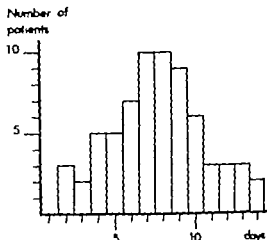


FIG. 1. Time between operation and phlebography in 68 patients with postoperative venous thrombosis. Mean 7.7 days.

due to deep vein obstruction are present in group B. A thrombus is usually not seen.

As different opinions concerning the phlebographic signs of fresh thrombosis exist, the main purpose of the investigation was to determine their relevance.

Material. This consisted of 72 phlebographies performed between March 1967 and July 1970. The majority of cases emanate from a material of postoperative thromboembolism (JANSSEN 1970 a, b). Only patients operated within two weeks previous to phlebography and in whom signs of thrombosis (criteria group A or B) could be detected were included. 72 legs, 31 right and 41 left legs, in 40 men and 28 women were examined. The age and sex distribution appears in Table 1. The average time between operation and phlebography was 7.7 days (Fig. 1) and between the onset of signs of thrombosis and phlebography 7.7 days, the latter in 49 patients (Fig. 2).

The onset of signs was not recorded in 13 patients and such signs were absent in 6 patients. None of the patients had signs before operation and it may be assumed that the onset of the thrombotic process usually started between operation and phlebography. The types of operations in the 68 patients were as follows: Biliary tract in 15, gastrointestinal tract in 23, urinary system in 28 (kidney, ureter and bladder in 11, prostate in 17), various in 2.

The signs and symptoms of venous thrombosis were roughly recorded and grouped as marked, moderate and slight. To the marked group belong cases with marked swelling combined with pain and discomfort. Local tenderness, sometimes combined with a certain amount of increased resistance of the deep tissues on palpation, was considered a slight sign. Cases with a slight increase

Number of patients

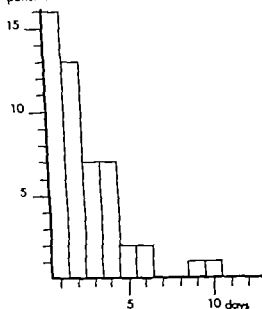


Fig. Time between onset of clinical signs of thrombosis and phlebography in 49 patients with postoperative venous thrombosis. Mean 2.7 day.

in the circumference of the calf (not more than 2 cm) without any other signs have also been referred to this group. The moderate group includes cases with intermediate signs that could not be referred to either of the other groups.

Five cases (legs) thus had marked 24 moderate and 35 slight signs of venous thrombosis. No signs could be recorded in 8 legs that comprised the positive cases in a material of postoperative phlebographies. Thus in 64 legs (62 patients) was a clinical suggestion of thrombosis an indication for phlebography while in the remaining 8 legs (6 patients) no clinical evidence of thrombosis was present.

Technique. Ascending phlebography was performed in accordance with the principles of Gærrtz (1954). Since the patients had just been subjected to operation the technique was sometimes modified. The examination usually started with the patient sitting with the lower leg vertical. A vein on the dorsum of the foot, preferably in the hallux, was punctured with a small needle and injected with 40 to 60 ml Urografin 60% or Isopaque Cerebral over 1 to 1.5 minutes; no tourniquet or elastic bandage was used. The patients were instructed not to contract the calf muscles when the leg was being examined. Two roentgen tubes produced alternative lateral and frontal projections with a horizontal beam. If the patient could manage to stand the examination was continued.

Fig. 3. Negative case. Ascending phlebography of leg. a) After injection of 30 ml contrast medium. b) and c) After injection of 60 ml contrast medium. Selective filling of deep veins (c) and subsequent filling of muscle veins (b). No tourniquet.



in that position. Films were first exposed of the lower leg and then of the region of the knee and thigh. If the patient could not stand up two films were obtained of the knee thigh region with a horizontal beam FFD 1.2 m. This technique demonstrated deep veins of the lower extremity and also provided optimal filling of the muscle veins of the calf (Fig. 3). The pelvic veins were not examined.

Complications. One patient died the day after the examination from pulmonary embolism. She was operated upon for carcinoma of the large bowel and autopsy revealed extensive thrombosis of both legs and multiple emboli in the lungs with total occlusion of the arteries of the right upper and the left lower pulmonary lobes. Any connection between the examination and the fatal outcome seemed unlikely. Some patients reported transient pain in the foot and the calf especially during the injection of contrast medium, sometimes with transient redness and swelling at the site of injection. No other sequelae have been recorded. Syncope never occurred during the examinations, probably due to the fact that the patients were sitting most of the time.

Results

Forty-six of the 72 legs in which thrombosis was evident from phlebography had constant filling defects (criteria group A) exclusively (Fig. 4). A combina-



F 4

F 5

FIG 4 Floating thrombus in muscle vein of the calf (→)

FIG 5 Cupola of thrombus (→) in the proximal part of the peroneal vein and non-filling of the vein distally

tion of filling defects and non filling of deep veins was present in 24 legs (criteria group A+B) (Fig 5). Non filling of deep veins (criteria group B) were the primary findings in only 2 legs.

The phlebographic location of thromboses related to clinical signs and roentgenologic criteria is presented in Table 2. It is noteworthy that phlebography in 18 of the 19 legs with muscle vein thrombosis of the calf demonstrated constant filling defects exclusively (criteria group A). Apart from muscle vein thrombus in the calf, phlebography in the remaining case revealed filling of several superficial veins in the thigh and fairly slow deep venous flow. These findings could have been due to existing iliac vein occlusion but since this region was not examined the case was classified as muscle vein thrombosis of the calf.

Non filling of deep veins and alterations in flow (criteria group B) were recorded in 14 of the 35 cases with leg thrombosis (cases with isolated muscle vein thrombosis in the calf excluded). In 3 of the 7 cases with leg thrombosis extending to the popliteal vein and in 8 of the 9 cases in which also veins of the thigh were affected. In all these cases except the two previously mentioned constant filling defects (criteria group A) were also recorded. The latter two cases will be described in detail: repeat examinations were performed in both. No filling of the distal part of the anterior tibial and the great saphenous veins occurred at the first examination in one of them but a further examination 53 months later revealed filling excepting for a 4 cm occlusion distally in the anterior tibial vein. Collateral veins were then observed. The patient had

Table 2

Location of fresh postoperative thrombosis in phlebograms related to signs and roentgenologic criteria in 77 cases (legs) no signs slight signs + moderate signs +++ marked signs 1 constant filling defects B non filling of deep veins

Location	N of cases	Signs				Roentgenologic criteria		
		-	+	++	+++	A	A+B	B
Superficial veins of calf	19	4	11	3	1	18	1	
Veins of lower leg and popliteal vein	35	4	19	1		21	13	1
Veins of lower leg and popliteal vein	7		3	3	1	4	2	1
Veins of lower leg and thigh	9		1	3	3	1	8	
Total	72	8	35	4	5	46	24	2

Cases with isolated muscle vein thrombosis excluded

received a drip infusion in the great saphenous vein of the ankle before the first examination. In the other case the first examination 5 days after operation disclosed collateral superficial venous flow only and no deep veins were filled. A further examination 7 days later demonstrated thrombi in the posterior tibial and popliteal veins and in muscle veins of the calf. No filling of the proximal part of the peroneal vein was evident and at the same level collateral veins were observed (Fig. 6). The patient at the time of the first examination had suffered from marked swelling of the lower leg and tenderness on palpation. The symptoms had almost totally disappeared at the second examination.

The thrombi were situated up to the level of or inferior to the popliteal vein in 63 of the 72 legs.

The relation between the roentgenologic criteria and signs and symptoms of thrombosis is apparent from Tables 2 and 3. Table 3 indicates that the two cases with roentgenologic criteria group B had moderate and marked signs respectively. None of the 46 cases with criteria group A had marked symptoms, most being slight. The 24 cases with criteria group A+B all had symptoms, most of which were slight or moderate.

Discussion

The literature suggests that phlebography is useful in the diagnosis of venous thrombosis, the general opinion being that constant filling defects in filled veins



Fig. 6 a) Non filling of deep veins of lower leg with rapid superficial flow b) After treatment and 7 da later visible thrombus in the proximal part of the posterior tibial vein

represent evidence of thrombosis. This view was held for instance by MAJOR et coll (1969) who during thrombectomy performed operative phlebography for the localization of thrombus formations and DIENER (1971) who carried out postmortem phlebography followed by careful dissection of the vein. A further sign of deep venous obstruction consists of changes in the flow with non filling of deep veins (NYLANDER). Both BERGVALL and BRODELUS et coll (1971) have by other phlebographic methods demonstrated that it is sometimes possible to demonstrate thrombus formations in cases with these indirect signs at ascending phlebography.

Table 3

Ascending phlebography in fresh postoperative venous thrombosis — no signs + slight signs ++ moderate signs +++ marked signs A Constant filling defects B non filling of deep veins

Signs of thrombosis	Roentgenologic criteria of thrombosis			Total
	A	A+B	B	
—	8	—	—	8
+	27	8	—	35
++	11	1	1	4
+++	—	4	1	5
Total	46	14	2	72



Fig. 7. Negative phase. Deficient mixing of blood and medium producing winding, incomplete filling defect (\rightarrow) in popliteal vein.

As to the question of fresh venous thrombosis, different authors have held divergent opinions concerning relevant roentgenologic criteria. The nomenclature also varies; as previously mentioned, the terms fresh and acute are often used synonymously (BOROSTROM *et coll.*)

NYLANDER stated that none of the deep veins are revealed at phlebography in acute thrombosis of the leg (criteria group B) and that filling defects (criteria group A) occur in the subacute phase, that is later on. BRODELIUS *et coll.* modified this statement by saying that group B changes occur in about 80 per cent of all cases of acute deep thrombosis of the leg and filling defects are demonstrated in the remainder. BOROSTROM *et coll.* and BECKER *et coll.* on the other hand considered that the only significant findings are constant filling defects (criteria group A). MAY & NISSEL have also pointed out that the earliest phlebographic sign of thrombosis is the outlining of the thrombus.

The term fresh thrombosis has been used in this report in conformity with BECKER *et coll.* and based on positive phlebographies performed in patients within 14 days of surgery. The observations diverge in some respects from those of NYLANDER, BOROSTROM *et coll.* and BECKER *et coll.* Seventy of the 72 legs had in fact constant filling defects (criteria group A) at the first examination in 24 in combination with non filling of deep veins sometimes with collateral flow (criteria group A+B). Phlebography at the first examination in only 2



Fig 8 Neeën case. Inconstant defect distally to h. m. popliteal vein (→) a) Frontal x b) Lateral x. The defect has disappeared

cases revealed indirect signs of deep vein occlusion (criteria group B) which NYLANDER gave as the most frequent finding in acute thrombosis. Neither can the observations of BOROSTROM et coll. MAY & NISSE and BECKER et coll. be confirmed completely as 2 cases of early thrombosis occurred without constant filling defects. The only roentgenologic signs in these cases were changes of flow at the first examination.

The reason why the present results in some respects diverge from those reported by the above authors cannot be explained with certainty. It might depend on differences in selection and composition of the materials for instance as regards the cause of the thrombotic process, its location and age, the phlebographic technique used and the clinical signs at the time of the examination. Only cases of postoperative venous thrombosis have been investigated. It cannot therefore necessarily be assumed that venous thrombosis from a different cause would produce similar phlebographic results.

The location and extension of the thrombus and its relation to the vessel wall ought to produce diverging phlebographic appearances. Floating thrombi with maintained flow at phlebography will obviously reveal filling defects. If on the other hand the thrombus be adherent to the vessel wall the phlebographic results will be dominated by non filling of the deep veins. The roentgenologic signs of thrombosis will thus vary with the degree of blockage of the vessel lumen.



Fig. 9. Negative contrast layering of contrast medium during filling of the muscle veins of the calf. a) After injection of 30 ml contrast medium, deficient filling of muscle veins. b) After injection of 60 ml contrast medium, visible defects (→) in muscle veins. c) The defects have disappeared.

The phlebographic findings also depend on a time factor or the stage of thrombosis at which phlebography is performed. From a pathologic viewpoint it is obvious that the older the thrombus the more easily it should be demonstrated; this refers to the recanalisation and retraction of the thrombus that may occur. These processes will be retarded by the presence of extensive damage to the endothelium (KAWAAN & ASTRUP 1965, BERTHESEN 1969). SCOTT (1968) has pointed out that retraction of thrombi and massive thrombolysis indicate the survival of the vessel endothelium. He reported partial retraction of primary occlusive experimental thrombi in rabbits at two hours. This clot retraction has been investigated experimentally by PIZA *et al.* (1967) who noted that the quantity of water in human blood clots during retraction decreases from 80 to 74 per cent during the first 24 hours after coagulation. The phlebographic technique may also be of importance in the result. The ascending technique performed in accordance with the principles of GRÆTZ probably ensured that venous thrombosis could be detected and that the significance of the findings

could be evaluated. The technique is also similar to those used by BORSTROM et coll, BECAER et coll, MAY & NISSEL and NYLANDER and thus this factor can hardly explain the different results.

This investigation supports the opinion given by BALER that floating thrombi produce few or no signs. Such thrombi were thus the only findings in the 8 cases in which no signs could be detected. Phlebography revealed constant filling defects only in those of the remaining cases without marked signs. This material also suggests that non filling of deep veins is usually combined with signs, probably on account of reactions of the vessel wall and the surrounding tissues as well as interference with the venous flow.

A connection between signs and symptoms of thrombosis and roentgenologic changes thus appears to exist. Cases with no or slight symptoms most often had changes of type group A. When changes of type group B existed exclusively or in combination with group A, the symptoms were more marked. Although criteria group B were sometimes recorded the dominating findings were criteria group A and thus the results mainly correspond to those reported by BORSTROM et coll and BECAER et coll. It seems reasonable to assume that the phlebographic signs of acute thrombosis described by NYLANDER (criteria group B) emanate from cases that had severe signs more frequently than in the present series, indicating real differences in the material.

The phlebographic diagnosis of venous thrombosis is based upon the presence of constant filling defects (BORSTROM et coll, DE WEESE & ROOFOFF, MAY & NISSEL and others). Several exposures at the same level will exclude sources of errors that depend on incomplete mixing between contrast medium and blood producing inconstant filling defects.

HJELISBERG noted winding contrast defects in filled veins in which blood free from contrast medium entered. These signs have also been described by EYSHOLDT (1964) who used the term inflow phenomenon for this deficient mixing of blood and contrast medium (Fig. 7). Filling defects distally to closed valves may also occur depending the layering of the contrast medium (Fig. 8). The injection of contrast medium in a slow blood stream will fill some vessels in a retrograde direction. This is a normal occurrence in the outlining of muscle veins (GRIFTZ 1955). The first films during the examination often reveal this layering of contrast to the most distal part of the muscle veins. The unmixed blood in the rest of the veins will then form a defect later disappearing with complete filling of the vein with contrast medium (Fig. 9).

There are also other sources of misinterpretations. ALMIEN & NYLANDER have demonstrated in serial examinations the emptying of the muscle veins by contraction of the calf muscles. Vein sections may be entirely compressed to simulate indirect signs of thrombosis. Deep veins may be compressed by a fracture

haematoma and oedema, producing non filling at phlebography (HJELMSTEDT & SUNDSTROM 1963 HJELMSTEDT & BERGVAL) Extensive superficial varices may complicate further examination of the deep veins GREITZ (1955) stated that a tourniquet around the ankle may result in non filling of the anterior tibial vein The injection of contrast medium into the great saphenous vein may also cause deficient filling of the deep veins

These false signs of thrombosis may thus be caused by (A) Inadequate mixing of contrast medium and blood producing inconstant filling defects (1) Defect from blood entering a filled vein (2) defect distally to a valve, (3) defect during the filling of a muscle vein (B) Non filling of deep veins for reasons other than thrombosis External or internal compression of the veins by muscle contraction bandages fracture haematoma and oedema Faulty technique These factors governing the relationship between contrast medium and blood as well as the obvious corollary that an unfilled vein may not be the same as one that is thrombosed should be carefully borne in mind and eliminated in the phlebographic diagnosis

Conclusions

Confirmation by pathology of a phlebographic investigation in man is difficult Only one case of this material was referred to autopsy and verified Cases with constant filling defects indicating thrombi can nevertheless be regarded as positive Indirect signs require a control examination to make the diagnosis more certain The most common phlebographic finding in fresh post operative thrombosis appears to be constant filling defects and the most common location is the lower leg Since positive findings were also recorded in cases with no or only slight clinical signs, phlebography ought to be in more common use, especially in clinically uncertain cases

SUMMARY

Ascending phlebographies in a material of 68 cases of fresh postoperative venous thrombosis of the lower extremity indicated that the most common roentgenologic signs were constant filling defects and that the main location was the lower leg An extended employment of phlebography especially in uncertain cases is suggested

ZUSAMMENFASSUNG

Aufsteigende Phlebographien bei einem Material von 68 Fällen mit frischer post operativer Venenthrombose der unteren Extremität deuteten darauf hin dass die gewöhnlichsten roentgenologischen Zeichen konstante Füllungsdefekte und die hauptsächlichste Lokalisation der Unterschenkel waren Eine verbreiterte Verwendung der Phlebographie besonders in unklaren Fällen wird vorgeschlagen

RÉSUMÉ

Des phlébographies ascendantes sur un série de 68 cas de thrombose veineuse post opératoire fraîche des membres inférieurs a montré que les signes radiographiques les plus fréquents sont des défauts de remplissage constants et que leur localisation principal est la jambe. Les auteurs proposent d'utiliser plus souvent la phlébographie en particulier dans les cas douteux.

REFERENCES

- ALLAN T and NYLANDER G. Serial phlebography of the normal lower leg during muscular contraction and relaxation. *Acta radiol* 57 (1962) 264.
- — False signs of thrombosis in lower leg phlebography. *Acta radiol Diagnost* 2 (1964) 345.
- BAUER G. A. angiographic study of thrombo-embolic problems. *Acta chir scand* (1940) Suppl No 61.
- Tidig diagnos av djup ventrombos. (In Swedish) *Svenska Lak Tidn* 64 (1967) 4041.
- BECKER J, BOROSTROM S and SALTZMAN G F. Occurrence and course of thrombosis following prostatectomy. A phlebographic investigation. *Acta radiol Diagnost* 10 (1970) 513.
- BIRCHALL U. Phlebography in acute deep venous thrombosis of the lower extremity. *Acta radiol Diagnost* 11 (1971) 148.
- BIRCHALL U. Reaction of the venous wall to experimentally induced thrombi. *Acta chir scand* 135 (1969) 491.
- BOROSTROM S, GRETTZ T, AN DER LINDEN W et coll. Ascending phlebography in fresh thrombosis of the lower limb. *Amer J Roentgenol* 94 (1965) 207.
- BROCKELUS Å, LÖNNQVIST P och NYLANDER G. Klmiska symptom och flebografiska fynd vid akut ventrombos. (In Swedish summary in English) *Nord Med* 83 (1970) 42.
- — Phlebographic techniques in the diagnosis of acute deep venous thrombosis of the lower limb. *Amer J Roentgenol* 111 (1971) 794.
- COOK W W and COLLIER F A. Clinicopathologic correlation in thromboembolism. *Surg Gynec Obstet* 109 (1959) 259.
- COTTON L T and CLARK C. Anatomical localisation of venous thrombosis. *Ann roy Coll Surg* 36 (1965) 214.
- DREIER L. Intravenous phlebography of the lower limb. Post mortem investigation of thrombotic venous disease. *Acta radiol* (1971) Suppl No 304.
- EYENOLDT K G. Beitrag zur Venenkontrastdarstellung bei akuten Abflussstörungen der unteren Gliedmaßen. *Fortschr Röntgenstr* 80 (1954) 714.
- FALLERUS G. Das Röntgenbild beim Vorliegen eines flottierenden Thrombus. *Acta radiol* 23 (1932) 444.
- FLAWO C, KAEKAR V V and CLARKE M B. Postoperative deep-vein thrombosis: Effect of intensive prophylaxis. *Lancet* 1969 I p 477.
- FORTAINE R. The John Hornum memorial lecture. Remarks concerning venous thrombosis and its sequelae. *Surgery* 41 (1957) 6.
- FRIEDMAN DAHL J. Postoperative Röntgenuntersuchungen. Diaphragmabewegungen und der postoperative Venenstrom. postoperative Lungenembolien. *Acta chir scand* (1935) Suppl N 36.
- GRETTZ T. The technique of ascending phlebography of the lower extremity. *Acta radiol* 42 (1954) 471.
- Phlebography of the normal leg. *Acta radiol* 44 (1955) 1.
- GULLMÅR Å. On the technique of phlebography of the lower limb. *Acta radiol* 46 (1956) 603.

- HÄGER K. Den kliniska trombosdiagnosen (o)tillförlitlighet (In Swedish) Svenska Lak Tidn 62 (1965) 1067
- and NYLANDER G. Acute phlebography. Triangle 8 (1967) 18
- HELLSTRÖM W O. Phlebographic studies and heparin treatment in thrombo-embolic diseases. Acta chir scand (1942) Suppl No 73
- HJELMSTEDT Å and BERGQVIST U. Incidence of thrombosis in patients with tibial fractures. A phlebographic study. Acta chir scand 134 (1968) 209
- and SUNDBLÖM R. Deep venous thrombosis following fractures of the tibial shaft. A phlebographic study of 40 patients one to two weeks after injury and after fracture union. Acta chir scand 126 (1963) 211
- JANSEN HJ (1) Prevention of venous thrombosis. Lancet 1970 I p 838
- (b) Dextran engångsdos som trombosprofylax inom allmänkirurgi (In Swedish) Nord Med 84 (1970) 952
- and ZACHRISSON B E. Postoperative thromboembolism and its prevention with 500 ml Dextran given during operation. Acta chir scand (1977) Suppl No 427 p 15
- KJELLBERG S R. Die Mischungs- und Stromungsverhältnisse an wasserlöslichen Kontrastmitteln bei Gefäß- und Herzuntersuchungen. Acta radiol 24 (1943) 433
- KWAAN H C and ÅSTRUP T. Fibrinolytic activity in thrombosed veins. Circulat. Res 17 (1965) 477
- LEA THOMAS M. Radiological diagnosis of deep venous thrombosis and its sequelae. Proc roy Soc Med 63 (1970) 123
- LINDBLÖM K. Phlebographische Untersuchung des Unterschenkels bei Kontrastinjektion in eine subkutane Vene. Acta radiol 22 (1941) 288
- MARANTA E und WIRTH W. Die phlebographische Lokalisation akuter und chronischer Venenverschlüsse und die Spontanrekanalisation thrombotischer Venenverschlüsse in phlebographischer Sicht. Zbl Phlebol 7 (1968) 7
- MAYOR G E, GALLOWAY J M D and MARIAPPY R G. Venography in iliofemoral venous thromboembolism. Surg Gynec Obstet 129 (1969) 57
- MAY R. Röntgenfrühdiaagnose der Thrombose. Zbl Phlebol 3 (1964) 143
- and NIMM R. Die Phlebographie der unteren Extremität. Georg Thieme Verlag Stuttgart 1959
- — Zur Symptomatik der frischen Thrombose der tiefen Beinvenen. Fortschr Röntgenstr (107) (1967) 262
- NEGLIS D, PRYTO D J, LE QUERRÉ L P et coll. ¹²⁵I labelled fibrinogen in the diagnosis of deep-vein thrombosis and its correlation with phlebography. Brit J Surg 55 (1968) 835
- NILSSON I M. The development of thrombosis. I. Thule International Symposium Stroke. Nordiska Bokhandels förlag Stockholm 1967
- NYLANDER G. Phlebographic diagnosis of acute deep leg thrombosis. Acta chir scand. (1968) Suppl No 387 p 30
- PIZZA F, GOTTLOW R and BLUMEL G. Zur Frage der Retraktion intra vital entstandener Blutgerinnsel. Klin Med 22 (1967) 97
- DOS SANTOS J C. La phlébographie directe. Conception, technique, premiers résultats. J int Chir 3 (1938) 625
- SCHWARTZ S I. Disorders of thromboembolic disease. In Special supplementary issue VII Congress of the International Cardiovascular society. J cardiovasc Surg (1965) Suppl No 132
- SCOTT G B D. A quantitative study of the fat of occluded red venous thrombi. Brit J exp Path 49 (1968) 544
- DE WEESE J A and ROGOFF S M. Phlebographic patterns of acute deep venous thrombosis of the leg. Surgery 53 (1963) 99

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THROMBOGENIC PROPERTIES OF VASCULAR CATHETER MATERIALS IN VIVO

A device and objective method of comparing thrombus formation
on vascular catheter materials

D SCHLOSSMAN

Synthetic materials are widely used in the manufacture of modern prosthetics such as heart valves, vessel grafts and shunts, although when brought into contact with the circulation they tend to give rise to thrombus formation and embolism. This drawback not only impairs their function but what is more, raises a serious risk to the patient. Thrombus formation on vascular catheters constitutes an analogous problem (JACOBSSON 1968) as thrombi form quickly on such catheters (SIGGELMAN *et coll* 1968, JACOBSSON *et coll* 1969, FORMANIK *et coll* 1970).

The side effect of contact of the blood with the surfaces of various vascular implants has produced extensive investigation into the thrombogenic properties of a wide range of synthetic products. The crucial tests have been performed in animal experiments, i.e. uniform pieces of various materials have been exposed to the circulating blood in a standardized way and the amounts of thrombi formed on them estimated and compared. The shapes of such pieces have varied

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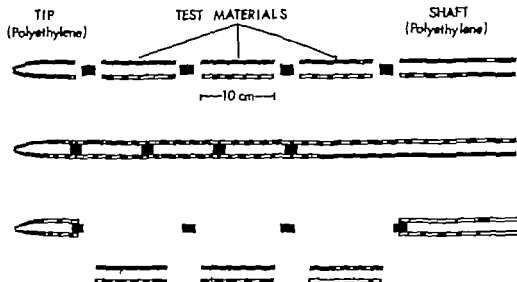


Fig. 1. Device for simultaneous formation of thrombi on various vascular catheter materials. Top: Before assembling. Middle: Assembled. Bottom: Disassembled for analysis.

widely from that of a teardrop to an atrial sword tube window ring or heart valve (MIRKOVITCH et coll 1964 SCHWARTZ 1965 GOTT 1966 BOCHER & BRAUNWALD 1967 DUTTON et coll 1968 JACOBS et coll 1968 CRODI et coll 1969). The amount of thrombi formed has been estimated in different ways although usually subjectively. The interval between the insertion of a tube or ring and its occlusion was however sometimes used as a measure of the thrombogenic properties of a particular material placed occasionally in arteries but usually in veins. The test periods in such experiments have ranged from hours to months; in the latter long term experiments only one substance has been tested at a time in each animal. The value of the results obtained in the investigations referred to has been limited by the poor accuracy of the methods themselves. A new device had therefore to be developed that permitted the simultaneous formation of thrombi on different vascular catheter materials; its usefulness was proved from the weights and isotope analysis of the thrombi formed.

Materials and Methods

The device. This was designed to lead to the formation of thrombi on more than one identically shaped piece of catheter material simultaneously. It was given the shape of a catheter intended for transfemoral insertion into the aorta

or inferior vena cava. The pieces of material were 10 cm long and were positioned between a 3 cm long tip and a 30 cm long shaft of polyethylene (Fig. 1). All the parts were of equal outer and inner diameter (according to the manufacturers 2.8 and 1.8 mm, respectively) and were united by 2 cm wooden pins, which thus also served as partitions between the lumina of the catheter pieces.

Since the thrombi on the outer surface of a catheter are wiped off on its withdrawal the device was designed in such a way as to permit thrombus formation on the inner surfaces of the pieces of material. All substances to be examined were therefore given 13 side holes 1.20 mm in diameter to allow a flow through them: the inner and outer surfaces of the catheters were thus also of equal area. When the devices were withdrawn from the vessel the deposits were readily available for analysis.

The individual catheter materials of which the device was composed consisted of one piece of each of the more common vascular catheters used in the department *viz.* teflon (Du Pont) polyethylene (Intramedic Clay Adams) and polyethylene with lead oxide (Ödman Ledin, KJFA).

Experimental procedure. Seven mongrel dogs weighing 12 to 23 kg were used. The platelets, fibrinogen and erythrocytes were labelled with ^{51}Cr , ^{59}Fe and ^{51}Cr respectively before the experiment proper. The dogs in a fasting state were placed on a warm table kept under light anaesthesia by repeated doses of thionembutal sodium (Pentothal sodium, Abbott) and given isotonic saline intravenously. One femoral artery and both femoral veins were gently exposed. One of the femoral veins was cannulated with a wide bore polyethylene catheter for blood sampling. One test device was then advanced into the aorta and one into the inferior vena cava. After a predetermined interval the devices were withdrawn and a fresh pair inserted. Identical devices were thus exposed simultaneously to arterial and venous blood for 5, 15, 30 and 60 minutes. The deposits on the catheter materials were weighed and their activities of ^{51}Cr , ^{51}Cr and ^{59}Fe measured. Samples of whole blood for measurement of radioactivity and for determination of the haematocrit, fibrinogen, red blood cells and platelet count were obtained before insertion of each pair of devices and again after the withdrawal of the last pair: there was one exception, namely after the insertion of the first pair which were in the vessel for only 5 minutes.

Isotopes. The day before the experiment the platelets were labelled *in vitro* with ^{51}Cr (250 μCi) by the method of AAR & GARDNER (1958) as modified by FOSS ABRAHAMSEN (1968). Dog fibrinogen was prepared from pooled mongrel ACD plasma according to BLOMBERG & BLOMBERG (1956) and labelled with ^{59}Fe (200 μCi) by the capillary jet technique of MCFARLANE (1956) as modified by LEANDORF *et al.* (1968). Erythrocytes were labelled *in vivo* by

Table

Weights of deposits after different periods of exposure to arterial and venous flow. Mean values of experiments in 7 dogs

	Arter.				Inferior vena cava			
	5 min	15 min	30 min	60 min	5 min	15 min	30 min	60 min
mg	16	608	588	611	438	647	620	59
SD	127	76	59	55	126	28	61	51

intravenous injection of $^{59}\text{Fe}(20\mu\text{Ci})$, ^{125}I fibrinogen as well as ^{59}Fe was injected 5 days before the experiment. Radioactivities of blood and deposits were measured with a 3" NaI well crystal (Autowell II Picker). The measurements were made on the main photo peak for each isotope and corrected for cross-talk between the isotopes.

Laboratory tests The mean of double determinations of the microhaematocrit was used. The platelets were counted by the method of BJORKMAN (1959) as modified by LJUNGVIST et al. (1971) fibrinogen being determined according to NILSSON & OLOW (1962). The red blood cells were counted in a celloscope (Celloscope 302 AB Lars Ljungberg Stockholm).

Calculation and statistical analysis Only total values for each device will be considered, i.e. all those given refer to the sums of the values for the three materials included in the device. Comparison of the values for each sort of substance will be the subject of a forthcoming article (SCHLOSSMAN 1972). The concentration of the isotopes in the deposits were calculated by placing the radioactivity of the deposits in relation to that of a corresponding weight of the blood from the sample obtained just before the test. Comparisons were made between pairs of observations in each animal by comparing the means of paired differences by Student's *t* test at the significance level of 0.05.

Results

Weights of deposits These soon reached a maximum, at which they persisted unchanged (Table). The increase in weight of the deposits in the artery reached this level within 5 minutes. When the device was placed in the vein the corresponding time was 15 minutes, from which time no significant differences were recorded between the weights of deposits formed in the arterial and venous flow.

Concentrations of isotopes in the deposits The greatest difference in composition between the deposits and the blood was the high ^{51}Cr activity of the

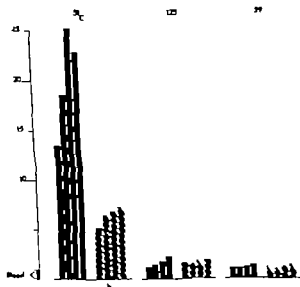


Fig 2 Activity of ^{51}Cr , ^{59}Fe and ^{125}I in deposits obtained after different periods of exposure (a=5 min b=15 min c=30 min d=60 min) of the device to arterial (■) and venous (□) flow in relation to the activity of the corresponding weight of blood arbitrarily set at 1. Mean values of experiments in 7 dogs.

former (Fig 2). The activity of ^{51}Cr in the arterial deposits was 13.4—25.2 times as high as that in the blood. The corresponding figures for the venous deposits were 5.1—7.2. The quotient between the ^{51}Cr activity in the deposits and that in the blood was much less (≤ 2.5). The ^{59}Fe activity in the deposits failed to differ from that in the blood; furthermore it was only in respect of ^{51}Cr activity that the composition of arterial deposits significantly differed from that of venous deposits.

The accumulation of the isotopes varied with the duration of the exposure. Thus the uptake of ^{51}Cr was highest in both arterial and venous deposits within 60 minutes. The accumulation of ^{59}Fe in the venous deposits was also highest within 60 minutes, while the concentration of this isotope in the arterial deposits increased only during the first 30 minutes.

General effects of the experimental procedure. The haematocrit, red cell count and ^{59}Fe activity did not vary during the experiments. The platelet count and the ^{51}Cr activity, however, dropped to 87 and 73 per cent respectively of their original values (Fig 3). Similar significant changes were recorded for fibrinogen and ^{125}I activity, which fell to 92 and 86 per cent respectively.

Discussion

A major difficulty encountered in tests hitherto used for comparing thrombus formation on different materials is to secure biologically similar conditions for

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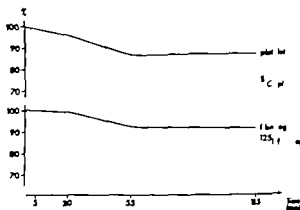


Fig. 3 Fibrinogen and platelets — labelled and unlabelled — in blood during experiments. Mean values of experiments in 7 dogs. Initial values set at 100 per cent.

the formation of thrombi because such a tendency varies between individuals and—after trauma, for example,—also in one and the same individual. The substances under test have often been implanted via a thoracotomy or laparotomy and only one piece examined in each animal. In other experiments different products have been tested consecutively in one and the same animal. Both procedures involve a risk of variation of the experimental conditions. The present method has not these drawbacks: it permits the simultaneous exposure of different materials to the blood and is much gentler than most surgical approaches hitherto used.

The device is such that it may be exposed to the blood stream for just a short time if desired. This is a great advantage because it would appear that the thrombogenic property of a given substance should be judged from its tendency to initiate thrombus formation. It has thus been demonstrated both clinically and experimentally that thrombi form rapidly on catheter material (SIZOGLIAN et coll., JACOBSSON et coll., FORMANEK et coll.) and that this formation is initiated by contact between the blood and the foreign body (JACOBSSON 1969, MUSTARD & PACKHAM 1970). It is, however, unknown to what extent the further development of the thrombi is influenced by or varies with the sort of material used. Moreover, thrombi soon undergo structural changes (MUSTARD & PACKHAM) and are also affected early by thrombolytic activity (JACOBS et coll.). In view of these considerations the observation periods in several investigations into thrombogenesis must be regarded as remarkably long: e.g. 72 hours to 22 days (MURPHY et coll. 1967), 14 days (GRODE et coll.) and 1 to 72 hours (SCHWARTZ).

The poor accuracy of the methods for quantifying thrombus formation seems to limit the value of many earlier investigations in this field. SAWYER et coll. (1970) for example simply noted whether thrombi developed or not, while

others (MURPHY et coll JACOBS et coll GLANCY et coll 1970) assessed such formation by a rough scale, e.g. thrombus grade 1 to 5

Of the two objective methods used in the present investigation i.e. weighing and isotope analysis the former proved to be an insensitive means of assessing thrombus formation apart from the inaccuracy of wet weights, the extent to which the deposits weighed consisted of thrombus blood or clots was uncertain. The weights also failed to demonstrate any notable difference between the deposits. Isotope analysis on the other hand confirmed that thrombi formed in the device since the deposits contained such an abundance of labelled platelets. The ^{51}Cr activity also best reflected the differences between deposits formed during different periods or in different vessels.

Though the composition of spontaneous thrombi in human beings probably varies widely (HENRY & HANLEY 1961) it has long been known that one major difference between arterial and venous thrombi is that the former are built up mainly of platelets. The difference in platelet content between these experimental arterial and venous thrombi thus agrees with that recorded in clinical investigations. The high ^{51}Cr content of the thrombi refuted the widely accepted belief (AMPLATZ 1971 HOSHAL et coll 1971) that deposits on vascular catheters are fibrin deposits.

It has been claimed that material tests in venous flow are severe ones for thrombogenesis (GORT). This may be true if the thrombotic mass and growth of the thrombus be used as criteria but the results of the present investigation suggest that if the platelet reaction elicited be used as a measure testing in arterial flow will be still more rigorous.

Analysis of the blood samples indicated (Fig. 3) that the conditions for thrombus formation changed in the course of the experiments. In a comparison of materials the test must therefore be performed simultaneously and not consecutively. The device presented provided excellent possibilities for this purpose and the amounts of ^{51}Cr labelled platelets proved most suitable for objectively quantifying and comparing the thrombus formation produced.

Acknowledgements

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SUMMARY

A device permitting the simultaneous formation of thrombi on three kinds of vascular catheter materials is described and its function evaluated in series of experiments in dogs. The weight and content of labelled platelets, fibrin and erythrocytes in arterial and

enous thrombi produced during different periods were investigated. The amounts of labelled platelets proved to be the most sensitive parameter for estimating differences between the thrombi.

ZUSAMMENFASSUNG

Ein Anordnung die die gleichzeitige Bildung von Thromben auf drei Arten von Material für eine kulture Katheter ermöglicht wird beschrieben und deren Funktion in einer Reihe von Versuchen an 7 Hunden geprüft. Das Gewicht und der Gehalt an gezeichneten Thrombozyten, Fibrin und Erythrozyten an arteriellen und venösen während verschiedener Zeiträume gebildeter Thromben wurden untersucht. Die Menge gezeichneter Thrombozyten erwies sich als der empfindlichste Parameter zur Feststellung von Unterschieden zwischen den Thromben.

RÉSUMÉ

L'auteur décrit un dispositif permettant la formation simultanée de thrombus sur trois types de matériaux constituant des cathéters artériels et il étudie le fonctionnement de ce dispositif sur une série d'expériences faites sur 7 chiens. Il a étudié le poids et la teneur en plaquettes marquées en fibrin et en érythrocytes des thrombus artériels et veineux produits à cours de différentes périodes. La quantité de plaquettes marquées paraît être le paramètre le plus sensible pour estimer les différences entre les thrombus.

REFERENCES

- AAS K. and GARDNER F. H. Survival of blood platelets labelled with chromium 51. *J. Clin. Invest.* 37 (1958) 1257.
- AMPLATZ K. A simple non thrombogenic coating. *Invest. Radiol.* 6 (1971) 280.
- BJORSEMAN S. E. A new method for enumeration of platelets. *Acta haematol. (Basel)* 22 (1959) 377.
- BLOMBAECK B. and BLOMBAECK M. Purification of human and bovine fibrinogen. *Ark. Kemi* 10 (1956) 415.
- BONCHIK L. I. and BRAUNWALD N. S. Thrombus resistant rigid prosthetic heart valves covered with porous synthetic fabric. *Trans. Amer. Soc. artif. intern. Organs* 13 (1967) 101.
- DUTTON R. C., BAILEY R. E., DEDERICK R. L. and BOWMAN R. L. Initial thrombus formation on foreign surfaces. *Trans. Amer. Soc. artif. intern. Organs* 14 (1968) 57.
- FORMANER G., FRUCH R. S. and AMPLATZ K. Arterial thrombus formation during clinical percutaneous catheterization. *Circulation* 41 (1970) 833.
- FOM ABRAHAMOV A. A modification of the technique for ^{51}Cr labelling of blood platelets giving increased circulating platelet radioactivity. *Scand. J. Haematol.* 4 (1968) 53.
- GLANCY J. J., FITHBONE G. and HENK E. R. Nonthrombogenic arterial catheters. *Amer. J. Roentgenol.* 103 (1970) 716.
- GOTT V. L. The causes and prevention of thrombosis on prosthetic materials. *J. Surg. Res.* 6 (1966) 274.
- GRODE G. A., ANDERSON S. J., GROTTA H. M. and FALW R. D. Nonthrombogenic materials via simple coating process. *Trans. Amer. Soc. artif. intern. Organs* 15 (1969) 1.

- HEYER R L and KASSEL M H Differences in thrombus formation and composition I Anticoagulants and fibrinolytics p 165 Edited by R L MacNellan and J F Mustard Lea and Febiger Philadelphia 1961
- HOMER V L JR ALLEN R and HOMER P A Fibrin sleeve formation on indwelling subclavian central venous catheters Arch Surg 102 (1971) 353
- JACOBSON L A KLOPFER E and GOTT V L Studies on the fibrinolytic removal of thrombus from prosthetic surfaces Trans Am Soc Artif Intern Organs 14 (1968) 63
- JACOBSON B Use of dextran in prophylaxis against thromboembolic complications in arterial catheterization Acta chir scand (1968) Suppl N 387 p 103
- Platelet adhesion and aggregation following contact between blood and vascular catheters in vitro Scand J Haematol 6 (1969) 216
- BERGQVIST S E and LUNGQVIST U Platelet adhesion and thrombus formation on vascular catheters in dogs Acta radiol Diagnosc 8 (1969) 221
- LEANDER L APPELQVIST L and BERGQVIST S E Fibrinogen turnover after massive haemorrhage in dogs treated with radioactively labelled fibrinogen Acta chir scand 134 (1968) 317
- LUNGQVIST U BERGQVIST S E and LEANDER L Platelet adhesiveness and aggregability after acute haemorrhage in the dog Acta chir scand 137 (1971) 1
- MCFARLANE A S Labelling of plasma proteins with radioactive iodine Biochem J 62 (1956) 135
- MEIKOWITZ V BECK R E ANDERSON P G and LERNER R I The zeta potential and blood compatibility Characteristics of some selected solids J surg Res 4 (1964) 395
- MURPHY P HOLLY F and SOMMER L BANKHOLE M SINOT S and BERNHARD W F Antithrombotic properties of electrified polymers Trans Amer Soc artif intern Organs 13 (1967) 131
- MUSTARD J F and PACHAM M A Thromboembolism A manifestation of the response of blood to injury Circulation 42 (1970) 1
- NILSSON I M and OLOW B Determination of fibrinogen and fibrinogenolytic activity Thromb Diath Haemorrh 8 (1962) 297
- NILSSON I M and OLOW B Determination of fibrinogen and fibrinogenolytic activity Thromb Diath Haemorrh 8 (1962) 297
- SAVIER P N SRINIVASAN S CHOPRA P S MARTIN J G LUCAS T BURROWS C B and SAUVAGE L Electrochemistry of thromboses—an aid in the selection of prosthetic materials J biomed mater Res 4 (1970) 43
- SCHLOEMAN D Thrombotic properties of vascular catheter materials in vivo Demonstration of differences between materials To be published in Acta radiol Diagnosc
- SCHWARTZ S I Biochemical factors affecting the production and prevention of thromboses Monographs Surg Sc 2 (1965) 159
- SIEGELMAN S S CAPLAN L H and AVERA G P Complications of catheter angiography Study with oscillometry and pullout angiograms Radiology 91 (1968) 251

NEPHROANGIOGRAPHY IN NEPHRONOPHTHISIS

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Nephronophthisis is a rare familial renal disease that affects children or sometimes young adults and always leads to uremia and death. The patient suffers predominantly from polydipsia, polyuria and fatigue and is pale, somewhat retarded in growth and has normal or often high intellectual capacity. Hypertonia is absent. Anemia, slight proteinuria, hypopotassemia, hyponatremia but no signs of pyuria, hematuria, bacteriuria, cylindruria, aminoaciduria or calciuria are evident. Microscopy of kidney tissue reveals diffuse changes with interstitial round-cell infiltration, dilated or atrophic tubuli, small cysts in Henle's loop or collecting tubules as well as much thickened basal membranes in the tubules and collections of connective tissue around Bowman's capsule, coloured by PAS staining. The cysts are usually less than 3 mm in diameter but may occasionally reach 4 cm. Diffuse atrophy occurs in the final stages chiefly in the cortex (FANCONI et coll 1951, HACKZELL & LUNDMARK 1958, IVERMARK et coll 1960, BROBERGER et coll 1960, GOLDMAN et coll 1966, HERDMAN et coll 1967, GLEASON et coll 1967, AXELSSON & ÖDLUND 1968, LINDBLAD et coll 1967).

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Urography is at first normal. After a while the kidneys shrink and the poor concentration of contrast medium finally renders demonstration of anatomic detail by urography impossible. Slight blunting of the calyces and uniform contraction of the kidneys may be observed with large doses of contrast medium (Siao et coll 1970).

Nephroangiography appears to have been performed in only 2 cases (MONROU & WORTHEM 1967). These had small kidneys with a thin cortex, poor demarcation between the cortex and medulla, enlarged medullary arteries and partial defects suggesting cysts in the medulla. We have performed nephroangiography during the last few years in 6 cases in which the clinical signs and histology of biopsy material have made a diagnosis of nephronophthosis highly probable.

Case reports

Case 1 Boy, aged 8, alert and doing well at school. No renal diseases in the family. Blood pressure maximum 135/115 (average 135/9). Anaemia present. ESR 60 mm, serum creatinine 2.4 mg/100 ml, hypotonic urine, low concentration capacity, slight proteinuria but no haematuria, pyuria or bacteriuria. Potassium excretion in urine was 60 to 80 mEq daily, serum 4.2 mEq/l. Histology of renal biopsy material (Fajana) indicated advanced periglomerular fibrosis, round cells interstitially, marked fibrosis and wide tubules. PAS staining produced strongly coloured basement membranes. Urography: Low contrast concentration but otherwise no abnormality.

Selective nephroangiography indicated that the kidneys were of normal size (10 cm × 6 cm) for the age. The cortex was thin (3 mm) and in the nephrographic phase not clearly distinguishable from the medulla. Several vessels at the periphery were bow-shaped. Rounded contrast defects were evident in the right kidney in the nephrographic phase and probably represented cysts in the medulla. The circulation rate was not disturbed.

Case 2 Girl, aged 19, student, intelligent. A sister had the same clinical condition and died in uraemia at the age of eleven. A cousin child died of nephronophthosis 1966. She had commenced to suffer from excessive fatigue with pain in the back. Two years later the serum creatinine was 2.5 mg/100 ml. Urography disclosed normal sized kidneys with no surface irregularities but enlarged calyces. Nephroangiography by contrast injection into the aorta appeared to be normal. Renal biopsy revealed periglomerular fibrosis, thin tubular epithelium and PAS positive material, peritubular interstitial fibrosis and a few round cells. A year after that the potassium content was 3.2 mEq/l, serum slight proteinuria but no pyuria, haematuria, bacteriuria, aminoaciduria nor calcium were evident, no hypertension nor oedema. Serum creatinine 3.3 mg/100 ml 1972.

Selective nephroangiography 1969 (Figs 1-2) demonstrated kidneys of average size. The cortex was somewhat thin (3 mm) but well-defined from the medulla in the nephrographic phase. The peripheral renal vessels were tortuous and in places bow-shaped. Numerous rounded contrast defects suggesting small cysts were evident in the nephrographic phase.



Fig. 1 Case . Right sided selective nephroangiogram. Cortex is thin and ill defined from medulla. Peripheral arteries in places bow shaped. Large cystic defect in the nephrographic phase (→)

Case 3. Girl aged 17, intelligent. A sister had died of chronic pyelonephritis at 10 years of age. A brother at the age of 15 had interstitial nephritis. On admission she was pale and had several bruises, normal blood pressure, anemia, serum creatinine $3.4 \text{ mg}/100 \text{ ml}$, serum potassium 2.9 mEq/l despite potassium substitution, slight pyuria but no hematuria, cylindruria or bacteriuria. Renal biopsy: Periglomerular fibrosis, PAS positive compacted fibrosis around atrophied tubules, focal interstitial fibrosis with lymphocytic infiltrate. Urography: Delayed weak secretion.

Selective nephroangiography (Fig. 3) indicated that the kidneys were of average size ($12 \text{ cm} \times 6 \text{ cm}$). The cortex was irregular and thin (0 to 3 mm) and at least partly ill defined from the medulla in the nephrographic phase in which numerous small rounded areas, rather poorly filled, were evident. The arterial branches in several places were bow shaped.

Case 4. Mechanic, aged 22, whose sister died at 11 of nephronophthisis. In 1968 he was considered slightly subnormal but not mentally deficient. He had hyperphoria and nystagmus, slight hypertension, anemia, serum creatinine $1.3 \text{ mg}/100 \text{ ml}$, normal serum potassium, slight proteinuria but no bacteriuria, hematuria or pyuria. Renal biopsy disclosed periglomerular fibrosis around some glomerules, marked atrophy of tubules, numerous interstitial cell formations and PAS positive structures around the nephrons of both the cortex and medulla. Hemodialysis was started in 1969.

Selective nephroangiography demonstrated rather small kidneys ($12 \text{ cm} \times 5 \text{ cm}$ and $10 \text{ cm} \times 4 \text{ cm}$). The left renal cortex was 2 mm thick with poor demarcation from the medulla; the right renal cortex was 4 mm thick. The peripheral arterial branches were narrow, tortuous and in places bow shaped. No definite defects were evident in the nephrographic phase.



Fig 2 Detail of Fig 1 b Numerous small cysts giving the parenchyma mottled appearance in the nephrographic phase

Case 5 Boy aged 17 intelligent. A brother had a similar renal disease and died of uremia when 16. For 1 year he had suffered from headaches, was tired and pale and had slight strabismus, myopia and anemiasis. He had no hypertension, no hypokalaemia, no slight pyuria predominantly of lymphocytic cells and no hematuria, proteinuria, bacteriuria or cylindruria. Serum creatinine was 3.5 mg/100 ml. Renal biopsy: Marked interstitial fibrosis, moderate inflammatory cell infiltration mainly from lymphocytes, elements atrophic tubules, peritubular thickening and thickening of Bowman's capsule. In PAS staining. Urography: Poor secretion but otherwise nothing abnormal.

Selective nephroangiography indicated that the kidneys were of average size (12 cm x 6 cm). The cortex was thinner than normal (3 mm) and well demarcated from the medulla. The peripheral arterial branches were of normal width and in places bow-shaped. A few contrast defects that might be cysts were evident in the nephrographic phase.

Case 6 Boy aged 14 in good condition but with proteinuria for eight years. His father died of interstitial nephritis and uremia and an uncle on his father's side had proteinuria. Proteinuria since 1964. Biopsy four years later disclosed wide tubules but no peritubular thickening with PAS staining. Serum creatinine was then 1.2 mg/100 ml. Urography: moderate widening and highly deformed calyces.

Selective nephroangiography 1968 and again 1972 demonstrated an average sized kidney on the left and but the right kidney was smaller than usual. The left renal cortex was 4 mm while the right was 2 mm thick. On both sides it was well demarcated from the medulla. The peripheral arterial branches were of normal width and in places bow-shaped. Defects possibly due to cysts in the medulla were evident in the nephrographic phase especially on the left side.



Fig. 3. Case . . . Left-sided selective nephroangiography. Cortex is thin and partly ill defined from medulla. Peripheral arteries bow shaped around large cyst-like defect (►).

A recent examination indicated that the boy had slight hypertension, serum creatinine 2.1 mg/100 ml, some proteinuria but no pyuria, hematuria, bacteriuria or hypopotassemia.

Discussion

The nephroangiographic examinations in these cases of nephronophthisis have revealed normal sized or in the later stages somewhat small kidneys with a regular outline and a thin cortex. The demarcation between the cortex and medulla varied in the different cases. Curved displacement of the peripheral arterial branches around the small rounded areas was usually evident here and there with defects in the nephrographic phase possibly representing cysts. These observations coincide in the main with those described by MONDEAU & WORTHEM, although 4 of our 6 cases had kidneys of normal size, the medullary arteries were never enlarged. The cortex in 3 cases was well demarcated from the medulla in the nephrographic phase.

The differential diagnosis between nephronophthisis and certain other renal diseases presents considerable difficulties. Some authors have considered nephronophthisis, medullary cystic renal diseases and diffuse interstitial nephritis one and the same condition (WINBERG 1964, STRAUSS & SOMMER 1967, PEDREIRA *et coll.* 1968, AXELSSON & ÖDLUND 1968), apparently by reason of similar histologic appearances. The similarity between nephronophthisis and medullary cystic renal disease is further indicated by the fact that in all cases of the former medullary cysts may be detected, at least microscopically. For

want of comparative angiographic material the present authors are not prepared to discuss the differential diagnosis between these two syndromes. However it must be emphasized that medullary cystic renal disease mainly occurs in adults and that the large losses of salt frequently encountered in this disease are not so prominent in nephronophthisis.

The resemblance between nephronophthisis and interstitial nephritis is emphasized by chronic interstitial nephritis being considerably more common in families with nephronophthisis than in the average population. Interstitial nephritis however chiefly affects adults. Angiographically there appear to be marked differences. The vascular displacements and contrast defect which in the present cases indicated the presence of cysts have had no equivalent in any of the 20 cases of diffuse interstitial nephritis angiographically examined and histologically verified.

The differential diagnosis between nephronophthisis and chronic pyelonephritis seldom presents difficulties. The characteristic calyx deformities evident at urography of chronic pyelonephritis are absent in nephronophthisis. Nephroangiography reveals more or less well localized areas of destruction of the parenchyma while reduction of the parenchyma in nephronophthisis is always diffuse even though the thickness of the cortex for example may somewhat vary.

The differential diagnosis between nephronophthisis and chronic glomerular nephritis is usually possible from the clinical examination. The sediment in the urine is characteristic and should prevent any mistake being made. On the other hand the differential diagnosis by angiography will not be obvious in those cases in which the demarcation between cortex and medulla is obscure; however even then the presence of cysts must suggest nephronophthisis.

The angiographic differentiation of nephronophthisis from polycystic familial renal disease in the late stages is easy. Difficulties of course occur if children with polycystic familial renal disease were examined at a stage when the kidneys were still of normal size.

SUMMARY

Nephroangiography of 6 patients aged from 8 to 22 years is reported. The diagnoses were based on the clinical condition and histologic examination of renal tissue. The angiographic findings are compared with observations published earlier. The differential diagnosis is discussed and the importance of angiography in this regard is evaluated.

ZUSAMMENFASSUNG

An sechs Patienten im Alter von 8 bis 22 Jahren wurde eine Nephroangiographie vorgenommen. Die Diagnose wurde auf Grund der klinischen Befunde und histologischen Untersuchung von Nierengewebe gestellt. Die erhaltenen angiographischen Befunde wurden mit

den bereits früher mitgeteilten Resultaten ergiebigen Differenzialdiagnose wird erörtert und der Wert der Angiographie diskutiert.

RÉSUMÉ

Les auteurs présentent les néphro-angiographies de 6 malades âgés de 8 à 22 ans. Les diagnostics étaient basés sur l'état clinique et sur l'examen histologique du tissu rénal. Les signes angiographiques sont comparés avec les observations publiées précédemment. Les auteurs étudient le diagnostic différentiel et ils examinent l'importance de l'angiographie à ce point de vue.

REFERENCES

- AXELSSON L. and ÖDLUND B. Cystic disease of the renal medulla and its possible relation to juvenile nephronophthosis. *Acta med scand* 183 (1968) 275.
- BRONKHORST O. WINKER J. and ZETTERSTROM R. Juvenile nephronophthosis. I. A genetically determined nephropathy with hypotonic polyuria and azotemia. *Acta paediat* 49 (1960) 470.
- ELLEN M. and BERNSTEIN J. Cystic diseases of the kidney—radiological and pathological considerations. *Clin Radiol* 20 (1969) 65.
- FANCONI G. HANHART E. ALBERTINI A. UHLINGER E. DOLIVO G. and PRADER A. Die familiäre juvenile Nephronophthosis. *Helv paediat Acta* 6 (1951) 1.
- GLEASON D. C. McALISTER W. H. and KIMMEL J. Cystic disease of the kidneys in children. *Amer J Roentgenol* 100 (1967) 135.
- GOLDMAN S. H. Walker S. R. MERRILL JR T. C. GARDNER K. D. JR and BILL J. M. C. Hereditary occurrence of cystic disease of the renal medulla. *New Engl J Med* 274 (1966) 984.
- HACKELL G. and LUNDMARK G. Familial juvenile nephronophthosis. *Acta paediat* 47 (1958) 428.
- HERDMAN R. D. GOOD R. A. and VERNIER R. L. Medullary cystic disease. Studies of an affected family. *J Pediatr* 67 (1965) 71b.
- LENNMARK B. LUNDQVIST A. and BARRY A. Juvenile nephronophthosis. II. A histological and microangiographic study. *Acta paediat* 49 (1960) 480.
- LUNDQVIST A. VICTORIN L. and WINKER J. Juvenil nefronofos. (In Swedish.) *Nord Med* 76 (1966) 1482.
- — — Atypical nephronophthosis. A clinico-pathologic study of juvenile patients without hypotonic polyuria. *Acta paediat* 56 (1967) 164.
- MANOGIS J. A. OPTER J. M. LURIE C. C. and COHEN D. U. Familial juvenile nephronophthosis. *Pediatrics* 34 (1964) 537.
- MONOGIS J. G. and WORTZMAN H. G. Nephronophthosis and medullary cystic disease. *Amer J Med* 45 (1967) 545.
- PEDRIZZA F. A. MARBER E. L. and BARSTROM W. H. Familial juvenile nephronophthosis and medullary cystic disease. *J Pediatr* 73 (1968) 77.
- SAO N. T. SWINGLE J. D. and GOMET F. Nephronophthosis. *Radiology* 95 (1970) 649.
- STRAUSS M. B. and SOMMER S. C. Medullary cystic disease and familial juvenile nephronophthosis. Clinical and pathological identity. *New Engl J Med* 277 (1967) 863.
- WINKER J. Correspondence. *Amer J Dis Child* 108 (1964) 566.

DYE DILUTION TECHNIQUE WITH NEPHROANGIOGRAPHY FOR THE DETERMINATION OF RENAL BLOOD FLOW AND RELATED PARAMETERS

JAN GOTHIN and TORD OLIN

Urography and angiography have long held a well established position in the diagnosis of renal disease, although information such as of clearance and flow measurements is however often required. Renal blood flow may easily be measured by an indicator dilution technique in connection with angiography. The present investigation was undertaken to evaluate the determination of such flow by this method, used as a complement to urography and nephroangiography.

Technique Indocyanine green (Cardio green Hynson, Westcott & Dunning Inc USA) in a concentration of about 25 mg in 35 ml distilled water was given in a single injection with a spring driven injector (Fig 1) made to fit a 1 ml disposable plastic syringe (Jintan Terumo Co Ltd, Japan) the injector could be set to deliver 0.3, 0.6 or 1.0 ml. The injection was initiated by pressing a trigger and automatically recorded on the potentiometer writer by a straight linear potentiometer and a capacitance circuit the injection rate

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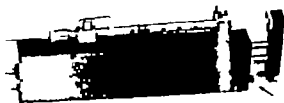


Fig. 1. The spring-driven injector with disposable 1 ml syringe. The trigger indicated (\rightarrow).

proved to be uniform. Control of the volumes delivered indicated a maximum deviation of ± 0.02 ml. In most cases 0.3 ml of the indocyanine green solution was injected in 0.15 to 0.20 seconds (rate 1.5 to 2.0 ml/s). The gain of the amplifier in the spectrophotometer was set at a fixed level.

As the analysing recording system was always calibrated after the examination by adding aliquots of the indocyanine green solution to a 10 ml blood sample, it was only necessary to vary the concentration of the dye from patient to patient to suit different flow conditions in the kidneys. The renal artery was entered from the femoral artery by a catheter (red Kifa—Ödman—Ledin I thin walled 60 cm, ID/OD = 1.5/2.2 mm) without sideholes. The tip was placed either 0.5 to 1 cm before the division into the ventral and dorsal arteries or central to the origin of the pole artery and was filled with indocyanine green solution before the start of the series of examinations.

The renal vein was entered from the femoral vein by a catheter (red Kifa—Ödman—Ledin I thin walled 80 cm long) with six sideholes within 1.5 cm from the tip. On the left side the catheter was placed with the sideholes peripheral to the probable origin of the spermatic or ovarian vein; a test injection of contrast medium sometimes demonstrated the site of the ovarian vein. The tip of the catheter had to be placed in a central branch of the main renal vein in some patients in order to avoid the inflow from the spermatic or ovarian vein. The blood from the renal vein was continuously drawn through the spectrophotometer cuvette (Oxi densitometer 351 Nycotron Norway) by a motor driven pump (Fig. 2) developed for the purpose, that can both aspirate blood and reinfuse it at a speed of 0.25 or 0.50 ml/s; usually the latter. The cuvette and its connecting tubes were sterilized by storing them in Ivolol (phenol derivatives in buffered solution) overnight. To avoid blood clotting the system was flushed before the series of examinations with saline containing 10 IU/ml



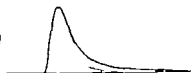
Fig. 2 The suction pump with 30 ml disposable syringe

heparin. The electric signal from the spectrophotometer was recorded on either a double channel potentiometer writer (Servogor Goertz Austria) with one linear channel and one logarithmic channel or on a single channel recorder (Electronik 194 Honeywell, England). A control indicated that the paper speed of the Honeywell writer (2.5 cm/s) was 0.3048 mm/s slow while that of the Servogor (1 cm/s) was 0.0052 mm/s fast. No corrections for these deviations were made. Every sample of blood was reinfused to avoid disturbances due to losses. In all 10 to 20 ml of blood were removed from the patient during the whole examination and used for the calibration.

Animal experiments with a white catheter (OPP 60 or OPP 160 Portex England) indicated that after blood had traversed the catheter indocyanine green adhered to the wall to give it a greenish appearance when red catheters were cut open and their inside walls brushed with gauze this also took on a slightly greenish colour. A lapse of at least 10 min was allowed between the green adhered to the wall giving it a greenish appearance when red catheters times performed after the latter. Three or four curves were obtained for each kidney. Although when these were dissimilar a few more were sometimes necessary. Calibration was made by adding 0.05 and 0.10 ml (sometimes 0.15 and 0.20 ml) of the indocyanine green solution to 10 ml of blood in heparinized tubes. The blood was drawn through the spectrophotometer at the same rate as that aspirated during the actual examination.

Calculation of the renal blood flow. The curve has been orientated so that the deflection at increasing concentration of dye is upwards. The method used in the present investigation to calculate the flow from the curves was described by LINDGREN *et coll.* (1969). The dye concentration curve usually reached the base line before the recirculation started but when this did not occur an extrapolation was made. With the double channel writer that of the downslope was made directly with the aid of the semilogarithmic curve (Fig. 3) but with the

Fig 3 D dilution curve from a normal kidney with semilogarithmic plotting of the down slope



Honeywell writer the extrapolation was performed on semilogarithmic paper and then plotted on the curve. The calculation was made with the Stewart Hamilton formula as follows:

$$q = F \int_0^{\infty} c_v dt$$

where

q = injected amount of dye (mg) F = renal blood flow (ml/s) c_t = concentration of dye in the renal vein blood (mg dye/ml blood) at time t

Adaptation of the formula to the present calculation of flow was described by LINGARDH *et coll* (1969) and EKELUND *et coll* (1972). In practice the calculations were those of LINGARDH *et coll*.

$$F = \frac{q D M_{100}}{M}$$

where

F = renal blood flow (ml/s) q = dye solution injected (ml) M_{100} = weight of 100 cm or 100 inches M = weight of the cut-out curve D = deflection in cm or inches on the potentiometer writer on calibration with 0.1 ml dye solution in 10 ml of blood

The flow through arteriovenous shunts was calculated as described by EKELUND *et coll*.

The centre of gravity of the cut-out curve was determined by suspending the plain curve from two different points and drawing vertical lines from them. The intersection of the two lines gave the centre of gravity which was projected perpendicularly onto the base line. The mean transit time was thus measured from the start of the injection to the projected centre of gravity, the delay in the analysing sampling and recording systems being subtracted.

Correction for the delay in the recording and sampling system. A venous sampling catheter of the same type and shape as that used in human subjects was introduced into the aorta of a rabbit in order to determine the delay in the appearance and mean transit times. Another catheter for injection of dye was placed with its tip close to the sampling catheter. Curves were obtained in the

Table 1

Renal blood flow, and mean transit time in kidney supplied by more than one renal artery

Case	Age	Sex	S	NoA	NoV	RA/D	IA	RBF	RBF/m	MTT	Diagnosis	Comments
1	24	M	L	2	1	d 4.5	3.8 d	436	227	8.1	Benign essential hypertension	
2	57	M	R	2	1	d 5.5	3.5 d	444	274	7.6	Normal	Malignant tumour of the ileum
3	24	M	L	3	1	v 1.0 d 3.8	4.1	454	256	9.9	Normal	
4	22	F	R	2	1	p 1.0	4.5	79+8	63	15.1	Amyloidosis	Shunt flow 8 ml/min flow in contralateral kidney 79 ml/min
5	63	F	L	2	1	p 2.2	4.5	248	142	8.2	Pyelonephritis	
6	45	M	L	2	1	p 1.0	4.9	253	148	9.2	Uncertain	
7	18	M	R	2	1	d 4.1 d	4.1	330	202	7.6	Glomerulonephritis acute	Shunt flow 317 ml/min
8	47	M	R	2	1	d a 3.4 d	4.1	336	170	11.3	Hypertension	Stenosis of left renal artery
9	41	M	R	2	2	d 3.9	3.8	280	146	7.3	Glomerulonephritis acute	
10	38	M	R	2	1	v d 3.8	3.8	223	117	6.5	Hypertension, disease and femoral artery	Sampling from renal branch in lower pole
11	31	F	L	2	1	p 2.1	4.1	229	140	10.5	Normal	

S Side of the kidneys injected

NoA Number of supplying arteries

NoV Number of draining veins

IA The artery injected v = central artery d = dorsal artery = renal artery p =
polar artery = intermediate artery

usual way and the delay in response of the writer was measured. The delay in the appearance time was 3.6 s, corresponding to the travelling time from the tip of the venous catheter to the spectrophotometer chamber. The delay in mean transit time was 5.6 s and represented the travelling time and the distortion caused by laminar flow in the collecting system. 3.6 and 5.6 seconds respectively have been subtracted from the measured distances in calculating the appearance and the mean transit times.

Abbreviations The following abbreviations will be used. RBF = renal blood flow in ml/min measured by the dye dilution technique. RBF/m = the renal blood flow in ml/min expressed as per m² of body surface. RAD = diameter of the renal artery in mm corrected by a factor of 0.75 to compensate for the magnification. S = the localization of the kidney examined, right (R) or left (L). VV = vascular volume in ml calculated as mean transit time \times flow in ml/s. VR = vascular resistance in peripheral resistance units (PRU) calculated as mean arterial pressure in mm Hg divided by the flow in ml/s. AT = appearance time measured from the beginning of the injection to the beginning of the curve with the delay in the sampling and recording systems subtracted. MTT = mean transit time in seconds measured from the beginning of the injection of dye to the centre of gravity of the cut-out curve set off perpendicularly on the base line with the delay in the sampling and recording systems subtracted.

Material A total of 44 kidneys were examined. 25 normal kidneys were investigated in 20 patients and of the remaining 19 kidneys 6 had compensatory hyperplasia. 11 were supplied by more than one renal artery and two demonstrated falling blood pressure during the blood flow examination series. The material is presented in Tables 1, 2, 3, 8 and 9. All kidneys were examined in connection with routinely performed angiography.

Results

Normal kidneys Seventeen kidneys without evidence of disease are presented in Table 2 and 8 kidneys considered possibly healthy in Table 3. The mean age of the first group was 37 years (range 15 to 61). Very old and very young patients have not been included. The mean renal artery diameter was 5.5 mm (range 4.5 to 6.8). 12 kidneys were on the right side. The mean total renal blood flow was 464 ml/min (range 405 to 527) while the mean renal blood flow per unit body area was 266 ml/min/m² (range 220 to 363). The mean vascular volume was 70 ml (range 46 to 96). The mean vascular resistance in

Table 2

Renal blood flow and related parameters in normal kidneys (group I)

Case	Age	Sex	RAD	S	RBF	RBF/m	VV	VR	MTT
1	42	M	6.0	R	470	70	64	23	9.2
2	40	F	5.6	R	435	72	69	7	9
3	54	M	4.5	L	494	254	86	18	11.6
4	18	M	5.8	L	480	294	74	22	9.2
	32	F	4.5	R	444	274	67	20	9.1
6	42	M	6.0	R	487	43	86	18	10.6
			6.8	L	461	230	70	19	9.1
7	55	M	4.8	R	47	160	5	22	7.8
			5.3	L	431	266	61	2	8.5
8	15	M	0	R	490	303	61	22	7
9	29	F	4.5	R	467	333	82	20	9.6
10	22	F	4.9	R	523	31	81	11	9.6
11	51	M	5	R	44	270	52	14	7.0
12	4	M	6.8	L	5.7	25	61	15	6.9
13	42	M	6.0	R	487	243	86	18	10.6
			6.8	L	461	230	70	19	9.1
14	61	F	5.2	R	40	256	46	17	6.8
Range	15-61		4.5-6.8		40 - 770	363	46	11-25	6.8 11.6
	17		17		17	17	17	17	17
Mean	37		5.5		464	66	70	15	8.9
SD			0.8		34.9	39.8	14.2	3.7	1.4
SE			0.2		8.5	9.7	3.4	0.9	0.3
			29.0		54.9	27.5	20.4	21.1	27.0

RAD Diameter (mm) of renal artery

S Side injected

RBF Renal blood flow (ml/min)

RBF/m Renal blood flow (ml/min per m of body surface)

VV Vascular volume (ml)

VR Vascular resistance (peripheral resistance units)

MTT Mean transit time (seconds)

peripheral resistance units was 19 PRU (range 11 to 25). The mean transit time was 8.9 s (range 6.8 to 11.6). The values of the kidneys represented in Table 3 are similar to those of the kidneys in Table 2. The greatest difference is in the vascular volume which is 59 ml in the latter material. Table 4 gives the mean values of both groups of kidneys considered normal.

The healthy kidneys in Table 2 are from patients in whom a search for primary tumours to pulmonary metastases was made haematuria due to

Table 3

Renal blood flow and related parameters in normal kidneys (group II)

Case	Age	Sex	RAD	S	RBF	RBF/m	VA	VR	MTT
15	16	M	6.8	R	319	1.0	42	28	7.9
			6.4	L	312	1.66	47	29	9.0
16	36	F	4.5	L	418	2.30	75	14	10.7
17	31	F	4.5	R	438	3.32	55	17	7.5
18	40	F	4.8	L	460	3.00	72	17	11.3
19	12	M	4.3	R	56	4.40	66	18	7.1
			6	L	492	3.90	69	21	8.4
20	53	F	5.3	L	300	1.63	46	30	9
Range	12-53		4.3-6.8		300-556	1.63-4.40	42-75	14-30	7.1-11.3
			8		8	8	8	8	8
Mean	31		5.3		412	2.74	59	22	8.9
SD			0.9		93.7	1.078	15.0	6.3	1.3
SE			0.3		33.2	0.382	4.6	2.2	0.5
			16.5		12.4	7.2	12.8	9.8	17.1

urethral bleeding pain in the back, a few in whom a pancreatic neoplasm was sought and one with orthostatic haematuria. Table 3 includes kidneys with bacteriuria before the angiography, haematuria with a normal angiography and a small cyst in the contralateral kidney.

The mean values of the RAD and RBF of male and female kidneys are presented in Table 6. The RAD and the RBF are larger in males but the RBF/m is the same in both sexes. The mean values of the right and left kidneys appear in Table 7. The mean RAD is larger in the left while the RBF and RBF/m is somewhat higher in the right kidneys.

The correlation $\log \text{RAD}/\log \text{RBF}$ was 0.2 $t=1.1$, the correlation $\ln \text{RAD}/\log \text{RBF}$ was 0.2 $t=1.2$ and the correlation $\log \text{RAD}/\log \text{RBF}$ was 0.2 $t=1.2$ (Table 5). No significant correlation was thus established.

Dye was injected into the renal artery on one side after the principal examination while blood was collected from the vein of the contralateral kidney in 3 patients. The deflection caused by recirculating dye always occurred after the concentration curve due to the first circulation through the kidney having reached the base line: no dye was measurable after a minute.

Multiple arteries. Eleven kidneys were supplied by more than one renal artery (Table 1). In cases 1 to 3, in which the largest of the feeding arteries was injected, the mixing of blood and dye was probably complete, as the flow

Table 4

Mean values of renal blood flow and related parameters (groups I and II)

		Range	SD	SE	t
No of kidneys	25				
Mean age	35				
RAV	54	43-68	0.8	0.2	33.9
RBF	448	300-526	63.2	12.6	35.4
RBF/m	268	165-440	66.8	13.4	20.1
VA	60	42-96	14.5	2.9	22.9
VR	20	11-30	4.8	1.0	20.9
MIT	8.9	6.8-11.6	1.4	0.3	33.0

value were within the normal range and no renal disease was present. In case 4 the value of RBF was the same on both sides, the shunt flow subtracted. The mixing of blood and dye was probably complete even in case 5 as the flow was within the normal range for a pyelonephritic kidney (GOTHLIN *et coll.* to be published). In cases 7 and 8 the flow values obtained after injection of indocyanine green into the dorsal and ventral arteries respectively differed which must be attributed to poor mixing. Case 9 had two renal veins on the right side. With catheters in the ventral artery and vein the flow was 280 ml/min (146 ml/min/m² of body area) and lower than expected; the patient had acute glomerulonephritis which is usually associated with an increased flow (GOTHLIN *et coll.*). Only recirculating dye could be registered with catheters in the ventral artery and the dorsal vein. When the catheters were placed in the dorsal artery and the ventral vein the results were similar. There was thus no mixing of blood at all between the two vascular compartments of the kidney. In case 10 one of haematuria and hypertensive disease, the distal end of the sampling catheter was introduced into a branch of a vein in the lower pole of the kidney and the mixing was probably poor. Dye was injected into the ventral artery which was 3.8 mm in diameter and the calculated flow was 223 ml/min (117 ml/min/m² of body area). Nothing abnormal was revealed either in the urograms or in the angiograms. Mixing must also have been incomplete in case 11 as the value of RBF/m² was too low for a normal kidney.

In summary the results obtained with the dye dilution method in kidneys supplied by more than one renal artery are uncertain, especially with more than one draining vein. If the kidney be supplied by a main renal artery and only a small aberrant pole artery and the injection of dye be made into the main artery the results may be reliable e.g. as in case 4 in which the flow of the other kidney was 79 ml/min.



Fig. 4. Aortogram in case 23 with compensatory hyperplasia of the right kidney (size 17.5 cm \times 17.5 cm)

Compensatory hyperplasia (Table 8 Fig. 4) Six patients had unilateral compensatory hyperplasia. Congenital hypoplasia on the contralateral side was diagnosed in 2, staghorn calculi in 2, carcinoma in one patient and scarring and shrinkage due to earlier nephritis in the remaining patient. The mean RBF was 610 ml/min (range 508 to 738), the mean RAD 6.5 mm (range 5.3 to 7.5) and the mean roentgenographic area of the kidney 85 cm² (range 61 to 107). According to MOELL (1961) normal value for males and females is 77 cm² (SD 13.6 to 15.6). The mean VV was 91 ml (range 68 to 123), the mean VR 15 peripheral resistance units (range 8 to 22) and the mean MTT 8.9 s (range 7.0 to 10.3). The angiograms demonstrated increased width of the renal artery and its branches, enlarged kidney size and a cortex slightly or moderately thicker than normal (Fig. 4).

Compensatory hyperplasia was associated with an increased RAD, increased thickness of the cortex and renal enlargement in the angiograms. The dye dilution investigation demonstrated an increased RBF and VV and decreased VR.

The effect on RBF of falling blood pressure (Table 9) The blood pressure fell during the dye dilution examination (140/60 to 100/60, 140/90 to 115/80 respectively) in 2 patients. The RBF/m² body area was lowered from 310 to 260 and 270 ml/min, and the VV from 64 and 83 ml to 35 and 57 respectively. The MTT did not change significantly. The reason for the fall in blood pressure

Tabl 5

Correlation of the diameter of the renal artery to the renal blood flow (groups I and II)

		t
RAD ₁₂₁₅ RBF ₁	0	1.0
RAD ₁₀₀₀ RBF ₁₂₁₅	0.2	1.1
RAD ₁₁ RBF ₁ s	0	1
RAD ₁₀₀₀ RBF ₁₀₀₀	0	1

was not known but vasovagal reflexes might have been the reason. The VR rose in both patients from circa 25 to 30 peripheral resistance units. Both kidneys in case 2 were normal at urography and angiography. The right kidney in case 1 exhibited pyelonephritic changes but the RBF measured in the left kidney was normal as were the urography and angiography.

Discussion

Methodologic problems. A clinical method should be as simple and standardized as possible which means that the number of unavoidable variables should be minimized to reduce the risk of error. A fixed coupling was therefore employed between the spectrophotometer, the amplifier and the writer. The amount of dye solution injected was varied from 0.3 to 1.0 ml in order to obtain a dye dilution curve of suitable height; these volumes are fixed on the automatic injector. As a second procedure the concentration of the indocyanine green solution (originally 25 mg indocyanine green in 30 ml distilled water) was changed. Injection by hand of 1.0 ml dye was performed in a few patients with a small RBF so that the injection rate would not exceed the flow of blood through the renal artery.

The only variable remaining was thus the amount of dye injected, one that was of course standardized. The calibrations of the spectrophotometer and the recorder were also standardized by means of a 10 ml sample of blood and the addition of 0.03 or 0.10 ml indocyanine green solution. It is important that the amount of blood and dye be correct and the admixture in the test tube complete. The exact concentration of the dye in the present method is of little significance. With a high sedimentation rate the blood and dye should be drawn back and forth through the system at least twice before the deflection is recorded. The suction pump should be driven by a motor of sufficient power as variations in suction speed influence the pattern of streaming through the spectrophotometer cuvette and thus change the optical density. The flow through the venous catheter is of the utmost importance if the flow be changed an

Table 6

Relation of renal artery diameter and renal blood flow in male and female kidney

	Male 9 right kidneys 7 left kidneys	Female 6 right kidney 3 left kidneys
RAD	8	4.9
RBF	455	434
RBF m	268	2.0

Table 7

Relation of renal artery diameter and renal blood flow in right and left kidneys

	Right 9 male 8 female kidneys	Left 7 male 3 female kidneys
RAD	5.0	3.6
RBF	4.9	431
RBF m	2.9	252

immediate and large distortion of the dye dilution curve will result. Such distortions occurred at the start of the investigation and a venous catheter with one endhole and two sideholes was replaced by one with one endhole and two sideholes. From then on only the latter type of catheter was used and no further sampling problems were encountered. The basic requirements for correct measurement with an indicator dilution method are that the renal blood flow be constant during the sampling, the mixing of indicator and blood be complete and no indicator disappears during its passage through the kidney.

The spectrophotometer is not entirely stable. Furthermore the values obtained are to some slight extent influenced by the oxygen saturation of the blood (LIN GARDH *et coll.*) blood for calibration should therefore be drawn from the renal vein.

BASSINGTHWAIGHTE *et coll.* (1962) and SAUNDERS *et coll.* (1970) proved in a model that overestimation of flow due to changes in the absorption spectrum was common if the appearance time of the dye was below six seconds. The uncorrected appearance time in the present material was never less. SHERRARD *et coll.* (1959) pointed out that distortion by sampling systems affects the dye dilution curves not so much in the shape as in the appearance time which may be delayed. The AT was slower by a mean of 3.6 s in the present investigation. SHERMAN *et coll.* (1959) also dealt with the distortion of dye dilution

Tabl 8

Renal blood flow and related parameters and renal artery diameter in compensatory hyperplasia

Case	Age	Sex	RAD	kA	S RBF	RBF/m	VA	VR	MTT	Diagnosis of contra Lateral kidney
21	27	F	d 5.6 5.8	107	R 738	4	123	8	9.9	Congenital hypoplasia
22	50	P	7.1	97	R 650	353	107	9	10.3	Staghorn calculus
23	56	M	7.5	104	R 617	321	97	13	8.9	Congenital hypoplasia
24	4	F	5.3	71	L 583	374	79	20	8.1	Staghorn calculus
25	64	M	6.8	72	R 331	32	68	19	7.0	Cortical scars—nephritis
26	5	M	5.6	68	R 308	299	79	22	8.3	Carcinoma 12 cm 12 cm
Mean			6.5	85	610	360	91	15	8.9	
Range			5.3—7.5	61—107	508—738	299—423	78—123	8—22	7.0—10.3	

Cross sect. renal area of the two renal cort. corresponds to one renal artery with diameter of 5.9 mm
kA Roentgenograph area of kidney

curves by sampling systems limiting their report to laminar flow. They found it difficult to compensate for small variations in the concentration of dye that may not be recorded. The present errors may be negligible especially with the Honeywell writer that reacts very fast. MILNOR & JONES (1960) observed that length, diameter and flow rate through the sampling tube each affected the curve independently but that the net effect of a combination of the variables could be expressed as a function of the ratio of volume to flow in the sampling system. The smaller the volume of the sampling system and the faster the flow through it, the less the distortion of the dilution curve. A volume to flow ratio of 0.5 or less was supposed to be a satisfactory practical compromise. These favourable conditions were not met in the present investigation but confirming the work of SHEPPARD et coll. it was mainly the appearance time that was influenced. The reliability of the dye dilution technique used to measure renal blood flow was established by LINGARD et coll. The ratio between flows determined simultaneously by direct collection of blood and by the dye dilution

Tabl 9

Renal blood flow and related parameters and renal artery diameter in 16 patients with blood pressure lowered during the vasodilation

Case	Age	Sex	RAD	S	RBF	AA	MTT	VR	BP
7	36	F	4.1	L	50	64	7.07	25	140/60
					485	57	7.07	27	170/60
					400	55	7.2	30	100/60
28	58	M	6.0	L	50	83	7.0	4	140/90
					680	75	6.5	25	170/80
					520	57	6.8	30	115/80

technique proved to be close to unit MEHRIZI & HAMILTON (1959) using a similar technique with Evans blue as the dye demonstrated good correlation without stating the figure.

Dye mixing. One of the basic requirements for dye dilution investigations is that complete mixing of dye and blood occurs before the sampling point. ØFSTAD *et coll.* (1967) demonstrated that the flow turbulence necessary for adequate mixing on the arterial side was produced by the injecting procedure. They further reported that when the curves from one kidney covered the same transit time but different areas this could be due to spill back of dye into the aorta. It is obviously important to have standardized dye injection: if the injection be too slow the mixing of blood and dye will be poor yet if too rapid some dye will spill back into the aorta. One way to obtain correct dye injection is to use an automatic injector such as a spring driven syringe; manual injection was employed only when the RBF was low.

LINGGARDH & LINDSTRÖM (1971) reported an extra ejection of dye amounting to 10 per cent with rapid injection, an aberration not observed with our syringe. The high normal values of the above mentioned authors (Table 10) may well be due to differences in injection technique. A rapid injection will furthermore result in some spill back of indicator into the aorta, yielding flow values that are too great. This cannot be tested with certainty by injecting contrast medium with the injector as the viscosity is too high.

Multiple renal arteries and veins. The kidneys supplied by more than one artery present various degrees of mixing of dye between the different compartments. Complete mixing probably occurred in cases 1 to 5 but in the remainder this appeared to be unsatisfactory. It is noticeable that in case 9 in which two renal arteries and veins were present, there was no mixing at all between the

Table 10

Renal blood flow and related parameters in normal kidney according to various authors

Authors	No. of kidneys	Technique	RBF Range /min	RBF Range	AA Range	VR Range	MTI Range
CORRYN & OLSEN (1952)	25	Single injection of dye	268	165-440	449	300-556	66.4-92 20 11-30 8.9 6.8-11.6
KARLSSON et coll (1967)	15		289	190-374	499	312-57	53 39-68 - - 6.5 4.9-9.4
KARLSSON et coll (1967)	5		238	180-304	- -	-	-
KOHLER et coll (1964)	21		329	±121	-	-	- -
LA SALLE & LUNDSTRÖM (1971)	12		325	261-443	570	451-768	- - - -
LOWENSTEIN & coll (1967)	8		350	19-1	607	512-888	57 23-56 - 4.55 3.4-5.6
RAZAKI et coll (1968)	15	Rad hippuric acid	- -	564	478-653	- -	- -
RENNI et coll (1966)	11	Single injection of dye	- -	592	400-1000	7 51-107	- - 9.2 7-13

two parts of the kidney. GRAVES (1956) stated that the arcuate veins anastomose and centrally situated anastomoses usually exist between the larger intrarenal veins and around the calyces. Under normal circulatory conditions, however, these intercommunications may be utilized to only a minor extent. Multiple renal veins appear in about 15 per cent of all kidneys (PICA & ANSON 1940). LUNDSTRÖM & LUNDSTRÖM (1971) reported that reproducible curves could be obtained when the catheter was inserted in different veins but their material may have been too small to reveal aberrations.

With only one renal vein present it may be possible to assess the total renal blood flow when the dye injection is made into one or two or more renal

arteries. Laminar streaming occurs in the renal vein however often prohibiting complete mixing. This stresses the importance of good mixing in the renal artery of kidneys supplied by only one renal artery where otherwise the same phenomenon may occur.

EDSMAN (1957) stated that about 21 per cent of all kidneys are supplied by more than one renal artery. BOIJSEN (1959) reported an incidence of 24 per cent. Many of these kidneys have only an extra pole artery. Dye dilution examinations of multiaarterially supplied kidneys have been made by COHN & GOMBOIS (1965). They obtained identical curves from the two arteries in one kidney and observed a close relationship between the dye dilution values and PAH clearance in another two. They also found kidneys with segmental venous drainage. KJOSCHOS *et coll* (1967) reported similar findings. Problems with poor mixing in multiaarterially supplied kidneys have also been described by SEALDON *et coll* (1962), REUBI *et coll* (1966), ØRSTAD *et coll* (1967) and LINGARDE & LUNDSTRÖM (1971).

The renal blood flow determined in kidneys supplied by more than one artery may to some extent be relied upon only if the value be close to that of the contralateral kidney and no obvious morphologic and functional differences are revealed by angiography.

Recording problems. Some of the distortion of the curves obtained at dye dilution examinations may depend upon the recorders. A certain sluggishness in this system does not noticeably affect the area of the curves but only their shape. The time lag to full deflection from the base line in response to an electric signal was 0.80 to 0.85 s in the Servogor potentiometer writer. For deflections within the range commonly used for the dye dilution curves the time taken for the deflection to reach its maximal point was 0.70 to 0.75 s and the time for the descent from this point to the base line was 0.80 s; both the ascending and descending limbs were nearly straight. In the Honeywell writer the time lag for deflection from the base line was 0.25 s within the working range and 0.37 s at maximum deflection. Full descent to the baseline took 0.50 s and within working range the descent time was 0.29 s. The sluggishness of the writer causes slight distortion of the curve. Copies of the dye dilution curves for integration should be made on stiff paper of even quality. Control weighting of 100 units of paper should be made at each determination as the air humidity may influence the weight.

Indocyanine green pharmacodynamic properties. CITERRIK *et coll* (1960) and HUNTON *et coll* (1960) gave surveys of the literature on indocyanine green and reported that there was no measurable extraction across the kidneys.

after the injection of the dye it was rapidly and completely bound to plasma proteins. It is rapidly excreted in the liver and in human subjects the plasma disappearance rate was 26 per cent/min with a dose as high as 0.25 mg/kg body weight. REUBI *et coll.* (1966) observed no significant absorption of free dye by the renal parenchyma of man.

Rabbit experiments with white catheters and examinations in human subjects in which the red catheters were cut open disclosed that indocyanine green is bound to proteins adhering to the catheter wall. The inner surface of the red catheters is about 25 cm² so this binding of dye to the walls may be of importance. It sometimes happened during the determination of renal blood flow that the first curve demonstrated a somewhat larger flow than the subsequent ones indicating a loss of dye. The arterial catheter should therefore be thoroughly rinsed with the indocyanine green solution before the start of the series of examinations so that the protein film adhering to the catheter wall be saturated with dye. No dye could be found on the walls of the venous catheter.

Medullary flow and recirculation. Several authors have stated that the down slope of the dilution curve does not follow the semilogarithmically extrapolated course. This has been attributed mainly to the slow non-cortical flow, e.g. the flow through the medulla, or to recirculating dye. The examination of 3 patients with injection of dye into the renal artery and sampling in the renal vein of the contralateral side clearly demonstrated that the recirculation in normal kidneys appeared after the original concentration curve had reached the base line; this has also been demonstrated in man by OFSTAD *et coll.* (1967) and by LINQARDH *et coll.* (1970) in dogs. That the medullary circulation is much slower than the cortical one has been suggested by many authors using a different technique (PINTER 1969). Thus the last deflection of the down slope of the curve is probably due to medullary circulation.

Mean transit time and vascular volume. The mean transit time was calculated in treating the curves but such entities as building up time and passage time were not measured; in only a few cases was the appearance time determined since these entities are felt to be much affected by the distortion due to the sampling and recording systems. The mean transit time is in common use and seems to be reliable (for references see ZIERLER). The analogue computer technique used to measure the mean transit time by determining the centre of gravity of the cut-out curve was conventional; this time was valuable in providing information about the vascular volume. This does of course vary with the position of the venous sampling catheter but volumes higher than normal were evident in compensatory hypertrophy as would be expected.

Renal blood flow related to the body surface The renal blood flow in the present investigation has been related to the body surface, which is a common parameter in medicine and probably a better reference than body weight. Other authors have related the flow to a body surface of 1.73 m² or 1.48 m² although it is better to reduce the flow to 1 m² as the standard body size of patients varies widely. Some authors have made no correlation at all of the renal blood flow with the body surface or body weight which makes it difficult to use their figures as references.

Single injections compared with continuous dye infusion The single injection technique has some advantages over continuous infusion of the indicator. It allows measurement of the mean transit time and permits estimation of the vascular volume; furthermore it is possible to estimate shunt flow and maybe medullary blood flow as well. The small amount of dye injected does not change the properties of the blood or its flow. Dilution of the blood may occur at constant infusion and yield dilution curves in the spectrophotometer (SEVERLAK et coll 1961). REUBI et coll (1962) stated that most experiments performed with a continuous technique produced false results.

The injection of dye should be as momentary as possible; in practice this means a small volume and rapid injection. If the injection rate be too high, spill back to the aorta will occur and the flow will be overestimated. This may be one of the reasons why some authors give higher values for the renal blood flow than those obtained in the present investigation; in several reports the volume of dye injected was more than one ml.

Dye dilution technique in comparison with other methods of measuring renal blood flow The most common method to determine the renal blood flow is to use a clearance technique, e.g. with PAH. This is difficult to apply in patients with shunts or oliguria for it demands measurements of the extraction and is unsuitable when the blood flow varies during the long sampling period, e.g. when the blood pressure is variable. Quantitative sampling of urine over a long period at a constant blood concentration is necessary. Inert gases are widely used, e.g. ¹³³Xe and yield reliable results (LEWIS & FARRINGTON 1968) if certain prerequisites are fulfilled. The position of the detector must be kept constant in relation to the kidney to avoid a false slope of the elimination curve and is best provided for by the kidney being exterior. The curve is dependent upon the partition constant between tissue and blood, which may be altered due to structural changes of the renal parenchyma, such as scarring and fibrosis. This fact is usually not considered in the calculations. Small variations in the slope of the curve may yield large differences in the calculated blood flow.

(REZUMI et coll 1963) With the gas diffusion methods the renal blood flow is calculated in ml blood/g tissue/min and the total blood flow cannot be measured. The dye dilution method is ideal to apply in connection with angiography. Its great advantages are that it gives the total renal blood flow independent of the weight of the kidney, it registers rather rapid fluctuations of the blood flow and is not time consuming. The effect of drugs exerting a brief influence on the kidney tissue may therefore be investigated. COIRA & GOMBOIS (1965) reported a dye/PAH ratio of 0.93 in 11 hypertensive patients. GOMEZ et coll (1965) recorded in various diseases good correlation between blood flow determinations made with the dye dilution technique and those obtained from PAH clearance. KJOSVOSK et coll (1967) gave the dye/PAH ratio in normal patients as 1.04 while REZUMI et coll (1966) reported a ratio of 0.87 ± 0.24 in normal patients and 1.09 ± 0.44 in chronic renal disease. LINGGARDH et coll (1969) observed the correlation between dye dilution and direct venous outflow measurements in dogs to be 0.95 and the correlation RBF_{dye} and $RBF_{HYPERTONIC}$ to be 0.88. The assessment of the renal blood flow is thus as accurate with the dye dilution technique as with other methods. Compared with inert gas methods it has the advantage that it is not necessary to know the weight of the kidney and with clearance methods (split function) the advantages are that catheterization of the ureters is unnecessary and rapid changes in flow may be registered.

BOLIN (1966) measured the blood flow densitometrically from angiograms. The method yielded somewhat high values for the renal flow and was technically difficult to perform.

OFSTAD et coll (1967) and LINGGARDH & LUNDSTROM (1971) reinfused the blood during the examination just as in the present material. REZUMI et coll (1966) prevented haemodynamic changes by giving blood transfusions during the examination. This means increased danger to the patient and may also influence the calibration. As small doses of indocyanine green both to prime the system and for the measurement were used in the present work the blood aspirated from the renal vein could if necessary be immediately reinfused. Some authors claim that it does not matter if the withdrawn blood be discarded but it would appear from animal experiments that the calibration is unreliable if the haematocrit decreases as may occur in human subjects if several samples of blood be discarded.

Effect of roentgen contrast medium on renal blood flow. LEITER (1965) demonstrated in man a transient fall in glomerular filtration rate and renal plasma flow after injection of contrast medium into the renal artery; the drop lasted not more than two minutes. APERIA et coll (1969) using a dye dilution technique in man described a variably marked fall in renal blood flow

The flow had returned to normal at the five and ten minutes controls. TALNER & DAVIDSON (1968) measured and reported a 10 to 20 per cent transient decrease in the renal blood flow after the administration of contrast media and of 4.5% NaCl whereas physiologic saline produced no significant changes. A time lapse of 10 minutes between the angiography and the dye dilution examination was usual in the present investigation. This is more than enough to avoid disturbances in the renal blood flow due to a previously injected contrast medium. Only minor and non-systematic variations in the flow were demonstrated in serial examinations.

Effect of the catheters on the renal blood flow GARZENSTEIN et coll (1962) with ^{131}I tagged serum albumin as an indicator established that the renal blood flow in man was not altered by the presence of catheters in the main renal artery. LEITER (1965) recorded a definite fall in the renal plasma flow in his patients while the renal artery was being catheterized but the immediate post-catheterization values were virtually the same as in the controls. LINDELL & OLIN (1957) catheterized the renal artery of dogs whilst measuring the renal blood flow by sampling the venous outflow from the kidney in a measuring cylinder. They reported no change in the flow after insertion of the catheter and the measurement of renal function by plasma clearance of phenol red in cats revealed no effect of catheter insertion into the renal artery unless spasm developed. BODORSS et coll (1964) reviewed the work of HELLANDER (1958) and maintained that his conclusions on renal function at catheterization of the renal artery in dogs were not valid. There is thus no reason to assume that the values of the blood flow obtained in the present investigation are lowered due to the influence of the catheter.

Renal blood flow, vascular volume, vascular resistance and mean transit time
The mean values of the normal renal blood flow are based on the findings in 23 kidneys from 20 patients. There was no angiographic evidence of disease in any of these kidneys and in the first 17 (Table 2) no clinical signs either. The second normal group (Table 3) contains angiographically normal kidneys in which there was some clinical evidence of disease previous to the examination. This group included patients with earlier haematuria and bacteriuria as the values of this group were similar to those of the first one they were placed together as a basis for determination of normal values (Table 4). KOHLER et coll (1964) examined patients with congenital or acquired cardiac disease without severe haemodynamic changes such patients may have impaired renal circulation. ORSTAD et coll (1967) measured the renal blood flow in 18 hypertensive patients with and without renal involvement and thought that a few of the failures in the dye dilution measurements might have been due to the low cardiac output in some of them.

Values for the renal blood flow and related parameters obtained in different investigations are presented in Table 10. Our values of RBF/m are in accordance with those of KJOSCHOS *et coll* (1967) while the results of KOHLER *et coll* (1964) LINGARDH & LUNDSTROM (1971) and LOWENSTEIN *et coll* (1967) form a group with higher values (330 to 350 ml/min/m body area). The values of RAZZAK *et coll* (1968) and REUBI *et coll* (1966) are not related to body area but their total values for the renal blood flow (564 and 592 ml/min) are higher than those in the present series. It is difficult to explain these differences but one reason may be the composition of the materials. There may for instance, be a variation in the condition of the kidneys between the series. It is always difficult to obtain an absolutely healthy material but at least in the first patients (Table 2) it was believed that this had been achieved. This group demonstrates homogeneous values the mean RBF/m of body area being 266 ml/min with a range of 220 to 363 ml/min. The values of vascular volume reported differed although this was to be expected as the position of the sampling catheter may play a considerable role the number and localization of side holes is also important. The low values arrived at by LOWENSTEIN *et coll* (1967) may be dependent upon their different method of calculating the mean transit time. The mean transit time in the present investigation was close to the values of REUBI *et coll* (1966) but higher than those of KJOSCHOS *et coll* (1967) and LOWENSTEIN *et coll* (1967). The mean transit time is of most interest in diseased kidneys.

The vascular resistance seems not to have received much attention in earlier flow investigations and no material of reasonable size has been located. Its relation to different diseases does however merit its calculation as will be evident in a later report.

In summary the present values of the renal blood flow were lower than in most other materials although those of the vascular volume and mean transit time were higher than in all others but one. The differences may be due to the composition of the materials various methods of catheterization and variations in equipment the premedication may be another factor. A standardized technique is necessary.

Male and female and right and left kidneys The normal material in the present investigation is small but a grouping has been made of male and female

Table 6) and right and left kidneys (Table 7). The larger mean renal artery diameter in right kidneys was surprising as MORILL (1961) reported that the left kidney was somewhat larger than the right and LINGARDH & LUNDSTROM (1971) that the blood flow of the left kidney (4 patients) somewhat higher than that of the right (8 patients). In an investigation of 30 diseased kidneys (GOTHLEN

et coll.) in which the blood flow determination and measurements of the diameter of the renal artery were performed bilaterally the mean diameter and mean renal blood flow were almost the same on the two sides. The composition and the small number of patients may account for the divergent results in the present investigation. The same may hold true for the difference in the mean renal blood flow between the right and left sides in patients with normal kidneys. On the other hand, as the ipsilateral spermatic or ovarian vein always enters the left renal vein although this occurs on the right side in only 12 per cent of patients, (AHLBERG et coll. 1967) the danger of blood from this vein passing into the sampling catheter by incorrect positioning is obvious. It may be that the flow of the right kidney really is higher than that of the left.

Effect of falling blood pressure on the renal blood flow. The blood pressure fell during the examination of 2 patients (Table 9). True shock did not develop and the patients recovered a short time after the withdrawal of the catheters. The state may have been due to vasovagal reflexes. The renal blood flow gradually fell and the vascular volume decreased. REUMI et coll. (1966) reported the same effect when hypotension was induced by the administration of hydralazine. INN LINGGARDH et coll. (1969) demonstrated in dogs that the renal blood flow diminished with the fall in blood pressure in acute haemorrhage.

It is thus evident that the renal blood flow of these two kidneys was dependent upon the systemic blood pressure.

Compensatory hyperplasia. SMITH (1951) reviewed the literature on compensatory hyperplasia and found that in both man and animals function increased as judged by the clearance of urea, diodrast, inulin and PAH. The weight of the kidney rose percentage wise to about the same degree as the function. The present investigation also revealed increased renal blood flow and vascular volume as signs of increased function. The mean roentgenographic area was 85 cm² compared with a normal value of about 77 cm² (MOELL 1961).

Relation between the renal blood flow and the diameter of the renal artery. The correlation, both linear and logarithmic, between these was low ($r=0.2$ and $t=1.1$ to 1.2) (Table 5). This is difficult to explain as good correlation exists in diseased kidneys (GÖTHLIN et coll.).

Conclusions

The blood flow through the kidney may be assessed only roughly by conventional nephroangiography. The diameter of the renal artery is not a reliable means of estimating the flow in healthy kidneys. Only specially designed

methods such as the dye dilution technique permit determination of the total renal blood flow. Glomerular filtration and tubular secretion are more or less dependent upon renal blood flow and may easily be determined by measuring the extraction of different substances if the total flow be known. Other methods of assessment of renal blood flow exist, or may be developed, although certain factors must always be borne in mind: the reliability of the method, the discomfort for the patient, the time taken for the examination and the radiation hazards for the patient and the examiner. The dye dilution technique deserves a position within the field of flow measurement and may advantageously be performed in connection with angiography of the kidney. It is not intended to replace the conventional roentgendagnostic procedures but complements them and thereby produces a more refined diagnosis and prognosis.

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SUMMARY

The renal blood flow, renal vascular volume, renal vascular resistance and mean transit time have been determined in 44 patients by dye dilution technique in connection with angiography of the kidney. The problems concerning this technique in kidneys supplied by single and multiple arteries are discussed. Normal values and those in kidneys with compensatory hyperplasia are presented.

ZUSAMMENFASSUNG

Die Nierendurchblutung, das Gefäßvolumen der Niere, der Gefäßwiderstand der Niere und die mittlere Verweilungsdauer wurden bei 44 Patienten mit Hilfe einer Farb-Verdünnungstechnik im Zusammenhang mit der Angiographie der Niere bestimmt. Die Probleme hinsichtlich der Technik bei Nieren, die durch eine einzelne und mehrere Arterien ernährt sind, werden besprochen. Normalwert und Wert bei Nieren mit kompensatorischer Hyperplasia werden gegeben.

RÉSUMÉ

Le débit sanguin rénal, le volume vasculaire rénal, la résistance vasculaire rénale et le temps de transit moyen ont été déterminés chez 44 malades par une technique de dilution de colorant en connexion avec une angiographie du rein. Les auteurs examinent les problèmes concernant cette technique dans les reins irrigués par des artères uniques et multiples. Ils donnent les valeurs normales et les valeurs pour les reins présentant une hyperplasie compensatrice.

REFERENCES

- ANDERSSON N, BARTLEY O, CHURCHILL N and WÄHLQVIST J. An anatomic and roentgenographic study of the renal vein in patient with and without renal carcinoma. *Scand J Urol Nephrol* 1 (1967) 43.
- ALLAN A, BROOKER JR O and LEPACHIN R. Renal hemodynamics during selective renal angiography. *Int. Radiol* 3 (1961) 389.
- ELMERHJELM J, EDWARDS A and WOOD J. Areas of dye dilution curves sampled simultaneously from central and peripheral sites. *J. appl. Physiol* 17 (1962) 91.
- POINTEUR B, MULLER I and OLIN J. Renal function test with radioactive diodrast in dogs. *Acta radiol. Diagnost.* 2 (1961) 431.
- Renal function judged with radio active diodrast selective renal angiography in dogs. *Acta radiol. Diagnost.* 2 (1961) 440.
- BOJER T. Angiographic studies of the anatomy of single and multiple renal arteries. *Acta radiol.* (1959) Suppl. No. 183.
- POINTEUR B. Contrast media in kidney during angiography. *Acta radiol.* (1966) Suppl. No. 27.
- CARRICK C, SMITH S, LEVY C and DAVIDSON C. Indocyanine green: Observations on its physical properties, plasma decay and hepatic extraction. *J. Clin. Invest.* 39 (1960) 597.
- COHEN J and CROWSON J. Indicator dilution method for measuring renal blood flow in man. *Amer. J. Cardiol.* 16 (1965) 870.
- FISMAN C. Angiography and suprarenal angiography. *Acta radiol.* (1957) Suppl. No. 122.
- FRIEDL D, GUTHRIE J and OLIN J. Arteriovenous fistulae in rabbit kidney studied by dye dilution technique and by splanchnic angiography. *Scand. J. Urol Nephrol* 6 (1972) 81.
- CARRICKER M, HICKS B, RYDER J et al. A new method of measuring renal blood flow. *J. Physiol.* 162 (1962) 21.
- COHEN D, DEMESTIERE M, SIEGHEVA J et al. Functional blood volume and distribution of perfused blood flow in the kidney of man. *J. appl. Physiol.* 20 (1966) 709.
- GUTHRIE J, HEDGECOCK V and OLIN J. Relations between blood flow, arterial non arterial area and total and cortical volumes of the kidney. To be published in *Acta radiol. Diagnost.*
- och OLIN J. Nefrosangiografi kompletterad med blodflödesmätning, radiografiska bildningsmetoden. (In Swedish.) *Nord. Med.* 84 (1970) 1317.
- CRILEY J. The anatomy of the intrarenal arteries in health and disease. *Brit. J. Surg.* 43 (1954-56) 606.
- HILFDER C C. Nephrographic effect and renal arteriographic damage. *Acta radiol.* (1958) Suppl. No. 163.
- HILFDER C C, LOISMA J and HOFFMAN. Hepatic removal of indocyanine green. I. Symposium on indocyanine green and its clinical application. *Proc. Mayo Clin.* 35 (1960) 7.
- KNOWLTON J, KIRKPATRICK W, VALENCA M and LITZ A. Unilateral renal haemodynamics and characteristics of dye-dilution curves in patients with essential hypertension and renal disease. *Circulation* 3 (1967) 229.
- KUNIGER M, BETTI J, BRÄUER H et al. Untersuchungen zur Bestimmung der Nierendurchblutung mit der Farbstoffverdünnungsmethode. I. Drittes Symposium der Gesellschaft für Nephrologie. Berlin S. 43. Verlag H. Vahlsberg, Berlin 1961.
- LEITER J. The effect of renal arterial catheterization on renal function in humans. *J. Urol.* 93 (1965) 6.
- LEWIS D and LEITZGROM A. Comparison of Xenon 133 washout curves from the kidney with direct measurement of renal venous outflow. *Scand. J. Urol Nephrol* 2 (1968) 62.
- LEWIS S and OLIN J. Catheterisation of the renal arteries in dogs and cats. *Acta physiol. Scand.* 39 (1974) 73.

- LINGGREN G and LUNDSTROM B Renal blood flow in man studied with a dye dilution method
In Studies on separate renal blood flow and function using a dye dilution technique and radiochemicals Scand J Urol Nephrol (1971) Suppl No 8
- MOTT T and OLIN T Renal blood flow in dogs studied by means of a dye dilution technique Scand J Urol Nephrol 3 (1969) 281
- LOWENSTEIN J, STEINMETZ P, EFFROS R et coll The distribution of intrarenal blood flow in normal and hypertensive man Circulation 35 (1967) 250
- MERUZZI A and HAMILTON W Effect of levarterenol on renal blood flow and vascular volume in dogs Amer J Physiol 197 (1959) 1115
- MILNER W and JOSE A Distortion of indicator dilution curves by sampling systems J appl Physiol 15 (1960) 177
- MOTIL H Kidney size and its deviation from normal in acute renal failure Acta radiol (1961) Suppl No 206
- OFFERD J, LUND JOHANSEN P and KOLBAKER L Dye dilution measurement of renal blood flow in vivo and in glass models Scand J clin Lab Invest 20 (1967) 281
- — — Dye dilution measurement of renal blood flow observations of the down slope of the dye dilution curve Scand J clin Lab Invest 20 (1967) 289
- OLIN T and GOTHELIN J Determination of renal blood flow in humans in connection with renal angiography Invited paper 12nd Congr Europ Am Radiol in Amsterdam June 16 1971 p 182 Excerpta Medica Foundation Amsterdam
- PICK J and ARNOY B Renal scula pedicle An anatomical study of 430 body halves J Urol 44 (1940) 411
- PRYTER G Measurements of renal medullary blood flow Experientia 25 (1969) 113
- RAZLAK M, BOTTI R, MACLENNAN J and PRITCHARD W Determination of renal blood flow by external monitoring of radioisotope disappearance J Urol 100 (1968) 209
- REINER E, EDEL H and BUONICCONTI E Critical appraisal of the measurement of renal blood flow using inert gas mixtures *In* Proceedings of the Second International Congress of Nephrology p 91 Excerpta Medica Foundation Amsterdam 1963
- REUBIN F, GOSWELER N and GURTNER R Renal circulation in man studied by means of dye-dilution method Circulation 33 (1966) 426
- GURTNER R and GOSWELER N A dye dilution method of measuring renal blood flow in man with special reference to the anuric subject Proc Soc exp Biol 111 (1962) 760
- SALDERS H, HOFFMAN J, NOBLE M and DOWEN CM R A source of error in measuring flow with indocyanine green Appl Physiol 28 (1970) 190
- SERADON S, HIGGS B, CHILMAN M I et coll Measurement of renal blood flow in man with the use of indocyanine green infused into the renal artery J Lab clin Med 60 (1962) 954
- SHEPARD C, JONES M and COOPER B Effect of catheter sampling on the shape of indicator dilution curves mean concentration errors mean flux of outflowing dye Circulat Res 7 (1959) 693
- SHERMAN H, SCHLANT R, KRAUS W and MOORE C A figure of merit for catheter sampling systems Circulat Res 7 (1959) 903
- SIMONSON J, SUTTERER W, FOX I and WOOD E Apparent dye dilution curves produced by injection of transparent solutions J appl Physiol 16 (1961) 669
- SMITH H The kidney Oxford University Press Oxford 1951
- TALNER L and DAVIDSON A Renal hemodynamic effects of contrast media Invest Radiol 3 (1968) 310
- ZIERLER K Circulation times and the theory of indicator-dilution methods for determining blood flow and volume *In* Handbook of physiology section 2 Circulation Vol I p 383 Williams and Wilkins Co Baltimore 1962

ARTHROGRAPHY OF THE KNEE

I Localization of lesions

H G RINGERTZ

The extensive literature on arthrography of the knee attests to the fact that lesions of the menisci and ligaments are frequently combined. The investigation by LINDBLOM (1948) was based on examinations performed during the period 1940—44 and STENSTRÖM (1968) published a report on combined clinical and radiologic findings in arthrography of the knee in children based on multiple discriminant analysis.

An attempt has been made to investigate the underlying traumatic mechanism and to classify combined ligament and meniscus lesions from the roentgenographic appearances alone. The computerized statistical evaluations have for reasons of comparison been applied to a complete series of 2 836 arthrographies of the knee performed during the five year period 1965—69. The investigations of the isolated and combined lesions of the same case material will be described in a paper to follow.

Material A total of 1 349 of the 2 836 examinations were regarded as pathologic from the radiologic point of view and subjected to statistical analysis. The age of the patients ranged from 15 to 80 years. Only the findings at the first examination were included if more than one arthrography had been performed on the same knee.

Table

Fields of re-entrations for statistical evaluation and number of possible findings for each appropriate entry

I Identification age sex and investigator			
II Performed operations	a) medial meniscus		78
	b) lateral meniscus		15
	c) cruciate ligaments		9
III Menisci	a) medial meniscus	1) anterior	247
		2) middle	447
		3) posterior	486
	b) Lateral meniscus	1) anterior	102
		2) middle	110
		3) posterior	47
IV Medial collateral ligament	a) femoral part		79
	b) tibial part		49
V Cruciate ligaments	a) anterior		519
	b) posterior		20
VI Other findings	a) fractures		26
	b) osteochondritis dissecans and free bodies		56
	c) Suda calcifications		10
	d) lateral collateral ligament ruptures		6
	e) capsul ruptures		4
	f) ganglion		2
	g) Baker cysts		20

Methods

Arthrography The arthrographic examinations were performed in the main according to LINDALOM. In addition anterior drawer lateral projections were invariably used. Posterior drawer lateral projections were however sometimes used for more detailed information on the posterior cruciate ligament. Additional ap views with flexed knee and 45° inversion and eversion of the leg were employed for the lateral meniscus when deemed necessary. The usual contrast medium was Urografin 30 % in an amount of between 12 and 17 ml.

Statistics A form was completed in each case (Table). Surgery in II had been performed before the initial roentgen examination and each entry in III, IV and V followed the classification given in Figs 1 and 2. The data were punched on cards, one card for each knee.

The lesions were divided as follows: (1) Meniscus lesions alone, (2) collateral ligament rupture alone, (3) cruciate ligament rupture alone, (4) combined meniscus and collateral ligament lesions, (5) combined meniscus and cruciate

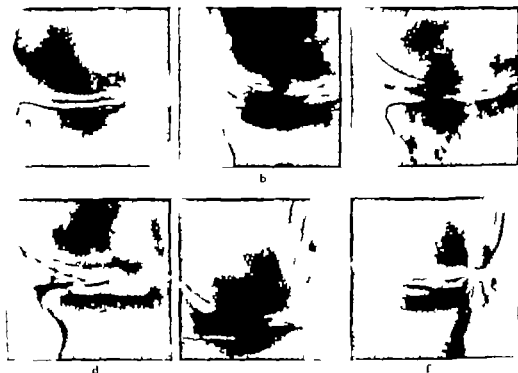


Fig. 1. Examples of the four types of ruptures in meniscus lesions and two types of localization of medial collateral ligament ruptures: a) vertical b) oblique c) horizontal and d) multiple meniscus lesions. Rupture: e) femoral part and f) tibial part of the medial collateral ligament.

ligament lesions, (6) combined collateral and cruciate ligament ruptures, (7) combination of (1), (2) and (3), (8) other findings. (1) to (3) have been called isolated and (4) to (7) combined lesions. Meniscus lesions included ruptured, defective and displaced as well as treated medial or lateral menisci. Collateral ligament lesions consisted of partial or total ruptures of both the medial and lateral ligaments directly demonstrated by arthrography or suggested from the presence of Stieda calcifications. Cruciate ligament lesions were made up of partial or total ruptures of the anterior or posterior as well as repaired anterior cruciate ligaments. For each subdivision and the whole material the sums of all detailed and field findings as well as age and sex distributions were calculated as a primary statistical survey.

Results

The number of positive findings for the different entries appears in the Table. The number of knees operated on was 98 which is less than the total individual operation entries due to surgery of more than one lesion in the same knee.



Fig. 2 Three degrees of cruciate ligament rupture: a) overstretched b) substantially ruptured and c) totally ruptured anterior cruciate ligament

Similarly the sums of knees with meniscus medial collateral ligament and cruciate ligament lesions of 757, 765 and 530 respectively, differ from the sum of the appropriate individual entries. The sizes of the combined groups of these main types of lesions according to the above given definitions appear in the Venn diagram (Fig. 3 a). The figure on each area represents the number of knees with the type of isolated or combined lesions as indicated by the localization within the three rings. These figures differ from the above totals as other findings and operations are included. The same type of representation of the material of LINDBLOM has been calculated for comparison (Fig. 3 b). The calculations were based on the figures given by LINDBLOM and the original material has not been reviewed.

The distribution by age and sex in the abnormal material appears in Fig. 4. The total number of females was 200 out of 1,349 cases representing 15 per cent and the percentage of females in the subdivisions of isolated and combined lesions varied between 5 and 21 per cent. There was a tendency to a higher representation of females in subsections (2) and (6) respectively. On the other hand subdivision (5) with combined meniscus and cruciate ligament lesions contained only 5 per cent of females.

The age distribution within the subsections did not differ significantly from that of the whole material. The percentage of patients above 35 years of age varied between 22 and 36 per cent in the subsections compared with 29 per cent for the whole material.

Discussion

The distribution of lesions, age and sex in a consecutive material always reflects special interests and restrictions. Patients over 50 years of age with meniscus or ligamentous lesions of the knee, are infrequently operated upon at this hospital.

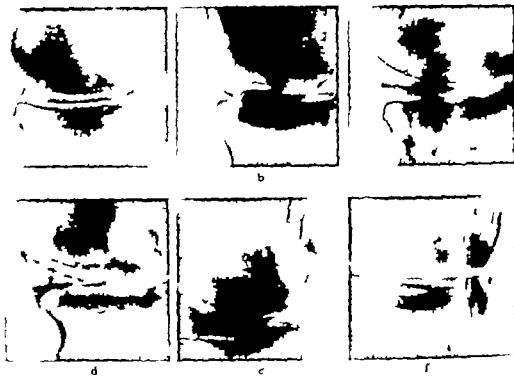


Fig. 1. Examples of the four types of ruptures in meniscus lesions and two types of localization of medial collateral ligament ruptures: a) Vertical b) oblique c) horizontal and d) multiple meniscus lesions. Rupture of femoral part (e) and tibial part of the medial collateral ligament (f).

ligament lesions (6) combined collateral and cruciate ligament ruptures (7) combination of (1) (2) and (3) (8) other findings (1) to (3) have been called isolated and (4) to (7) combined lesions. Meniscus lesions included ruptured, defective and displaced as well as treated medial or lateral meniscus. Collateral ligament lesions consisted of partial or total ruptures of both the medial and lateral ligaments directly demonstrated by arthrography or suggested from the presence of Stieda calcifications. Cruciate ligament lesions were made up of partial or total ruptures of the anterior or posterior as well as repaired anterior cruciate ligaments. For each subdivision and the whole material the sums of all detailed and field findings as well as age and sex distributions were calculated as a primary statistical survey.

Results

The number of positive findings for the different entries appears in the Table. The number of knees operated on was 98 which is less than the total individual operation entries due to surgery of more than one lesion in the same knee.

so that few appear in the material. The special interest in repair of the anterior cruciate ligament (LILJEDAHN et coll 1965) is also reflected in the series.

The comparison between the two materials of equal size from the same hospital collected in 1940—44 and 1965—69 presented marked differences. In the earlier material the meniscus lesions dominated but later the three groups of meniscus, collateral ligament and cruciate ligament lesions were of about the same size. This affects essentially the combined lesions, a fact which reflects an increased interest in the diagnosis and repair of ligament lesions as well as greater traumatic forces exerted on the knees.

The three main types of lesions represent a characteristic dominance of the defect present at the following sites: the medial meniscus, the upper part of the medial collateral ligament and the anterior cruciate ligament. The findings confirm those of RICHTER et coll (1971).

The distribution of age and sex in the different lesions was about the same as that of the whole material. A statistical test that compared the sex distribution in the age group 20 to 24 years with the rest of the material revealed a significant preponderance of males in the group than would be expected from the number of females in the group. The reason for this probably lay in the effects of military service and athletic activities.

SUMMARY

The findings in 1349 abnormal cases out of 2836 arthrographies of the knee performed during a five year period have been evaluated statistically. Compared with the situation prevailing 25 years ago, marked increase in combined meniscus and ligament lesions was evident, probably partly reflecting higher traumatic forces involved in the injuries.

ZUSAMMENFASSUNG

Die Befunde von 1349 abnormalen Fällen bei 2836 Arthrographien des Knies, die während einer Fünfjahresperiode ausgeführt worden waren, wurden statistisch bearbeitet. Verglichen mit der Situation vor 25 Jahren war ein markanter Anstieg von kombinierten Meniscus- und Ligamenteschäden deutlich, welcher teilweise die schwerere Natur der Unfälle widerspiegelt.

RÉSUMÉ

L'auteur a étudié statistiquement les résultats de 1349 cas anormaux sur 2836 arthrographes du genou faites au cours d'une période de cinq ans. Par comparaison avec la situation qui existait il y a 25 ans, l'auteur a observé une nette augmentation des lésions combinées des ménisques et des ligaments, reflétant probablement en partie la plus grande intensité des forces traumatiques intervenant dans les traumatismes.

REFERENCES

- LIJEDAL S O, LIND ALL N and WETTERFORS J. Early diagnosis and treatment of ruptures of the anterior cruciate ligaments. *J Bone Jt Surg* 47A (1966) 1503
- LINDBLOM K. Arthrography of the knee. *Acta radiol* (1948) Suppl No 74
- RICALLY P, RUTTMANN A and DEL BUONO M. Meniscus lesions. Practical problems of clinical diagnosis, arthrography and therapy. Second edition. Crane & Stratton, New York, 1971
- STENSTROM R. Arthrography of the knee joint in children. Roentgenologic anatomy, diagnosis and the use of multiple discriminant analysis. *Acta radiol* (1968) Suppl No 481

NON PREGNANT ANATOMY OF THE POSTERIOR ABDOMINAL WALL AS REFLECTED IN THE COURSE OF THE OVARIAN VESSELS AND URETER

Roentgenographic, statistical and anatomic investigation

LARS OHLSON

The recognition of certain anatomic relationships in the abdomen is a prerequisite for an analysis of the changes occurring there in pregnancy. These relationships have therefore been investigated by the roentgen examination of the ovarian vessels and the ureter and by dissection of the organs and structures of the posterior abdominal wall with special reference to their mobility. Dissections were performed by LEONARDO DA VINCI in about 1510 and documented in a series of drawings that depict the ovarian vessels passing in a straight course medial to the ureter and in front of the external iliac vessels to the ovary where they turn upwards to the uterine horn; both vessels are single. HUNTER (1774-1794) demonstrated the anastomoses of the ovarian, uterine and round ligament vessels in pregnancy and in an investigation of the nerve supply of the uterus in non pregnant subjects dealt with the connective tissue sheath surrounding the ovarian vessels in the posterior abdominal region. SOULIGOUX (1894) described the ovarian artery as being tortuous along its entire course and the vein as consisting of several branches in the pelvis forming a single straight vessel at the pelvic inlet. The ovarian vessels in text books of anatomy (CONNINGHAM 1938, TESTUT & LATARET 1949, CORNING 1949, PATURET 1958) are

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briefly described as passing along the psoas muscle crossing the ureter at a slight angle, and entering the broad ligament in front of the common or external iliac vessels. The accounts of the iliac vessels are however too disparate to afford any precise information about the topography of the ovarian vessels at this level. Thus in several drawings, both TESTUT & LATAJET and PATURET represent them at the pelvic inlet as passing 1 to 2 cm lateral to the ureter while in others at least 3 cm from it.

These descriptions made no suggestion of asymmetry of the ovarian vessels. PERKOPF (1964) however represented them on the right side as crossing the whole psoas muscle, thus reaching the quadratus and iliac muscles, where they turned caudally to pass behind the ileo caecal valve. On the left side they ran close to the lateral aspect of the psoas muscle to the lateral border of the intersigmoid recess. Their further course was symmetric and they entered the pelvis at the lateral border of the inlet 4 to 5 cm lateral to the ureters.

The above mentioned authors failed to offer any account of the configuration of the ovarian artery but it was depicted proximal to the ovary as almost straight and distal to it as more or less tortuous. The branches of the pampiniform plexus of the vein are said to join into one or two veins above the inlet, but no information was offered about the site of the confluence. TESTUT & LATAJET and PATURET represented this site in some drawings as being just above the inlet while in others two or three branches extended almost to the cranial collecting veins and intercommunicated at several levels.

The origin of the ovarian artery examined by HASELHORST & SCHILLING (1926) in 50 autopsy cases was located at the level of the second lumbar vertebra in 70 per cent of cases. The angle between the artery and the spine estimated by these authors in 27 cases, proved to be the same on both sides. TESTUT & LATAJET depicted in a large number of drawings the arteries as arising close to the anterior midline of the aorta and descending symmetrically. The right had a precaval course, though this does not necessarily indicate asymmetry. Similar accounts were presented by CUNNINGHAM (1937), CORNING (1949) and PATURET (1958). According to CUNNINGHAM however the artery occasionally follows a retrocaval course. ELISKKA (1961) described the ovarian arteries arising from the aorta as passing behind the vena cava in at least 6 per cent of cases.

The authors referred to give no descriptions of the medial, para aortic division of the retroperitoneal space beyond conventional accounts of the topography. The topography emerges in greater detail from certain drawings of transverse sections where the vena cava occupies almost the entire space between the parietal peritoneum and the paravertebral structures. The homologous left space with the same sagittal size as the right, is filled with fatty areolar tissue. MILLOY et coll. (1962) examined the venous system on each side of the abdominal aorta in

an autopsy material, and stated that the variations on the right side were small, while on the left side various degrees of persistence of the left vena cava were present.

The ovarian artery was first demonstrated by arteriography by DOS SANTOS (1931) in two cases of large uterine fibroma. BORELL & FERNSTROM (1934) in a series of ovarian tumours, salpingitis, and tubal pregnancy demonstrated that the configuration of the part above the inlet was almost straight while distally the artery became tortuous. FRATES (1969) made similar observations in cases of ovarian and trophoblastic tumours.

Material. The roentgenographic series comprised the ovarian artery in the 37 non-pregnant cases presented in a previous report (OHLSON 1972), the ovarian vein in 31 normal abdominal arteriograms and the ureters in 21 normal urograms in women aged between 18 and 40 years.

The post mortem dissections comprised 100 ovarian arteries arising from the right side and 100 arising from the left side of the aorta.

Methods

Roentgen investigation. The courses of the ovarian vessels and the ureter were recorded in the coordinate system as described in a previous report (OHLSON). The courses of the vessels and the ureter were defined by the normal of their contours in the *a-p* plane. The artery was divided by various topographic points into a number of parts (Fig. 1). Below the level of origin of the artery, two parts of the vein corresponding to parts 2 and 3 of the artery could be distinguished. The transition between parts 2 and 3 was at level 0.0 of the *y* axis. The configuration of the artery was examined as to the distribution along its course of three kinds of distinctive figures: curves, axials and loops.

Dissections. The ovarian vessels on each side were accessible to inspection and palpation through the parietal peritoneum below the root of the mesentery and the sigmoid colon respectively. On the right side these conditions were present cranially as well, except in a few cases in which the structures were partially covered by the root of the mesentery or the ascending mesocolon. The parietal peritoneum was then freed by deflexion of the mesentery without dissection. On the left side the descending mesocolon covering the ovarian vessels and the ureter was freed by dissection with a minimum of manipulation. The consistency and mobility of these structures in relation to one another and to the peritoneum and the posterior abdominal wall were examined by pressure and traction. The configuration of the artery was then examined by palpation and traction and the mode of attachment of the ascending and descending mesocolon by traction and direction.

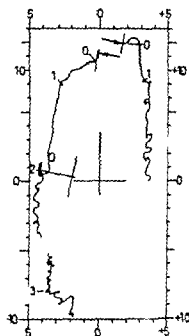


Fig. 1 Course of ovarian artery in a single case. Topographic points indicated. Scale 1:3. Inner wall of aorta (\rightarrow).

The para aortic division of the retroperitoneal space was defined as comprising the structures on either side of the aorta, its lateral extent corresponding to that of part 1 of the ovarian artery. The presumed anterior midline of the aorta was defined: the peritoneum removed and the attachment to the spine of the aorta and vena cava and their branches examined. The aorta was then incised in the presumed anterior midline and the internal origins of the ovarian and lumbar arteries examined. Since the distance along the internal circumference of the aorta from the presumed anterior to the posterior midline proved equal on the two sides the anterior midline was defined as such. No attempt to determine the form of the transverse section of the aorta was made.

Results

Röntgen investigation. The courses of the ovarian vessels and the ureter appear in Figs 1, 2, 3 and the Table. The course in the para aortic section corresponding to part 1 of the artery is further dealt with in a report that follows (OHLSSON, to be published).

The course of the artery was symmetric, passing caudally into the pelvis without significant deviations: the artery turned near the ovary in a medio-crudal direction to the anastomoses. The vein, being filled from the left renal venous system, could be examined only on the left side: its course coincided with that of the artery (with no significant difference at any level).

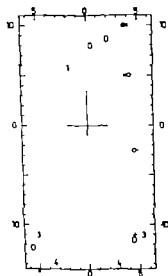


Fig. 2 Course of ovarian artery, ovarian vein and ureter in the coordinate system. Topographic points marked: ovarian artery \circ , ovarian vein \times , ureter. Scale 1:4.

The course of the ureter converged slightly on the two sides ($p < 0.001$). On the right side, it was more lateral at levels $+5.0$ and $+2.5$ of the y axis although without significant asymmetry. This meant that the right ureter crossed the artery distal to part 1 between levels 5.0 and 0.0 while the left ureter crossed the ovarian vessels within part 1. At the inlet corresponding to the level -2.5 the ureter passed 0.9 cm medial to the artery on the right side and 1.3 cm medial to the ovarian vessels on the left side ($p < 0.001$).

The configuration of the artery was bilaterally more tortuous in part 3 than in part 2. The frequency of the distinctive figures was for part 2 on the right side 2.2 and on the left side 1.8; for part 3 on the right side 16.9 and on the left side 15.1. (For part 2 on the right side: 24 curves, 4 axials and 3 loops ($n = 14$); the corresponding values on the left side being 26.6 and 1 ($n = 18$); for part 3 on the right side 118.39 and 12 ($n = 10$) and on the left side 62.25 and 4 ($n = 6$)). The increase in tortuosity occurred near the transition between parts 2 and 3 (Fig. 3a). A corpus luteum was filled in 17 cases, invariably in the secretory phase (Fig. 4).

A branch to the right renal capsule in one case arose from part 3; it had the same width as the artery proximal to the site of branching while that of the artery distal to that site was less. No other branches from parts 2 or 3 filled. Branches from part 4 to the tubes were generally outlined. In no case could any change in width of the artery distal to the site of branching be demonstrated. The width was less than in pregnancy ($p < 0.001$).

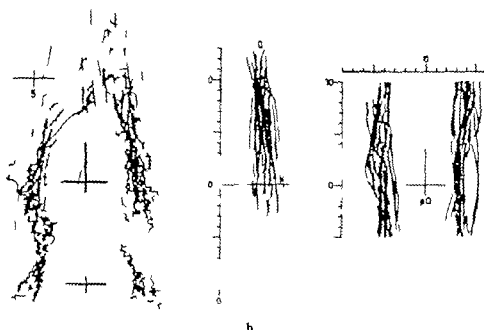


Fig. 3 Superposed course records of ovarian artery (a) ovarian vein (b) and rete (c)
 Scale 1:4

The configuration of the vein was consistently almost straight (Fig. 3b). Its width in the a.p. plane varied by less than 1 mm in all except 2 cases, in which it varied between 6 and 8 mm, and 10 and 13 mm, respectively. The vein in 3 cases was double below the levels of 9.5, 5.5 and —0.7 respectively; the branch was straight in contradistinction to the branches of the pampiniform plexus.

Dissections. The ovarian artery always arose from the anterior wall of the aorta on each side at a distance from the midline of 1.5 to 4 mm, generally 2 to 3 mm. Its internal origin was fine, regular and sharply delimited from the wall of the aorta which was considerably thicker and firmer. The angle between the ovarian artery and the aorta was small; the artery first passed adjacent to the external aortic wall beneath the aortic sheath which it gradually penetrated to become surrounded by its own sheath.

The artery on the right side was precaval in 78 cases and retrocaval in 23 cases. The precaval arteries were interposed between the peritoneum and the vena cava in a thin layer of areolar tissue that contained solitary lymph glands. The arteries and the glands were readily displaceable. The sheath of the vena cava was much thinner than that of the aorta. The artery was almost straight or slightly tortuous and reached the anterior aspect of the ovarian vein at the confluence of the vein and the vena cava. The shape and consistency of the retro-

Table

Course of ovarian artery, ovarian vein and ureter. Mean values, standard deviations and number of cases for coordinates at different levels of y axis

Level of y axis	Ovarian artery						Ovarian vein			Ureter					
	Right			Left			Left			Right			Left		
	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n
100	18	1	5	37	0.9	11	37	0.4	18	40	0.5	9	40	0.5	15
5	29	14	7	38	0.9	18	40	0.6	18	45	0.5	19	40	0.7	20
0	57	14	16	42	0.8	23	4	0.6	31	45	0.6	21	38	0.7	20
+25	42	13	13	45	0.7	20	44	0.7	24	43	0.7	21	35	0.7	19
00	47	13	17	47	0.9	19	46	0.9	15	40	0.7	21	35	0.6	20
-5	46	0.7	13	49	0.8	13	46	0.7	9	37	0.6	19	35	0.7	18
30	39	12	16	47	0.9	9									

caval space was similar to the precaval space the arteries and the glands being readily displaceable the mobility of the arteries was however limited by their passage between the subsequent levels of the confluences of the lumbar veins and the vena cava. The configuration of the arteries was similar to that of the precaval ones they joined the ovarian veins at the right wall of the vena cava.

The para aortic section homologous to the section containing the vena cava was on the left side situated in front of the lateral aspect of the spine and psoas muscle. It was filled by areolar tissue and lymph glands. Longitudinal communications between the lumbar veins were common but invariably much smaller than the right vena cava they communicated with the renal and ovarian veins. This part of the ovarian artery was embedded in fatty tissue and covered by the fatty descending mesocolon. Its configuration varied from almost straight to tortuous and its course was in all directions more variable than on the right side a cranial and dorsal course being relatively more frequent.

The ovarian vessels and the ureter passed caudad in the areolar tissue between the psoas muscle and the peritoneum of the posterior abdominal wall the ovarian vessels slightly diverging the ureters slightly converging. The right artery and vein joined close to the right wall of the inferior vena cava and met the ureter about 1 to 3 cm distal to that site while on the left side the three structures came together within part 1 of the artery. The vessels on the two sides then passed in front of the ureter to which they gradually became more lateral at the inlet they generally lay immediately lateral to the ureter in no case more than 2 cm and in about 30 per cent of cases in front of the ureter.

The diameter of the artery was about 2 mm ranging from 1 to 4 mm and

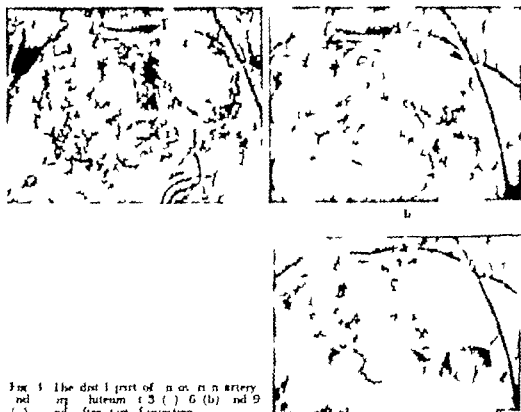


Fig. 5. The distal part of an ovarian artery and vein: (a) before, (b) and (c) after tartar injection.

the width of the vein in its collapsed state was generally 4 to 5 mm, ranging from 3 to 12 mm. The artery coursed along the frontal aspect of the vein. Part 1 of the artery was almost straight or slightly tortuous while part 3 varied from being slightly tortuous to convoluted but was always more tortuous than part 2. Three kinds of distinctive figures could be identified: curves, axils, and loops. The configuration of the vein was always almost straight. The artery reached the medial or lateral border of the vein and passed 1 to 2 mm outside it for short stretches corresponding to its tortuosity. When the vein was distended by blood from communicating veins, some curves and circles of the artery became perpendicular. The artery never wound round the vein. The pimpliform plexus generally extended 2 to 3 cm above the inlet and in about 10 per cent of cases 1 to 5 cm above the inlet. Higher than this level the vein was a single vessel sometimes receiving a small affluent from the sheath of the ureter. The ovarian vessels entered the broad ligament at the pelvic insertion of the suspensory ligament of the ovary running in turn in the edge of reflection of this fold, the mesovarium and the edge of the ovarian ligament.

The ovarian vessels were surrounded by a common sheath of a thickness and firmness similar to that of the ureter. When traction was applied to the peritoneum of the posterior abdominal wall, the vessels followed the peritoneum for 2 to 3 cm. but on further traction gradually became detached from it. The ureter followed the peritoneum in a similar manner but retracted more easily. Thus when, for instance, the caecum or the lateral lower part of the sigmoid colon was pulled laterally, the ovarian vessels became separated for several centimeters from the ureter. The parietal peritoneum could be elevated into folds extending in the direction of traction in which the vessels or the ureter could readily be elevated. Extension and elevation of the broad ligament gave rise to a peritoneal fold in the abdominal wall in the border of which the ovarian vessels passed. When the extension ceased the artificial fold disappeared and the ligament resumed its former position. Digital compression through the parietal peritoneum readily displaced the ovarian vessels and the ureter 3 to 4 cm. between the peritoneum and the muscles and with increasing pressure still further. The ovarian vessels could be separated from one another but this required greater compression or traction than for separation of the vessels from the ureter.

The vessels in the borders of the suspensory and ovarian ligaments were less mobile than above the inlet, their most fixed site being the mesovarium where the peritoneal layers of the broad ligament were attached. The layers in all other regions were mobile in relation to one another, the one connecting into the other at the edge although less readily than the parietal peritoneum. Separation of the layers near the edge by traction occurred less readily than separation of the parietal peritoneum from the muscles while towards the pelvic floor the layers could be separated as easily as the parietal peritoneum from the muscles.

The root of the mesentery and the mesocolon of the right side could be readily loosened from the peritoneum by deflecting the mesentery in a lateral cranial and anterior direction whereas on the left side the fatty descending mesocolon was fused to the peritoneum and permanently attached by its continuity with the rectum. The ligamentous connections between the caecum and the peritoneum were attached above the pelvic inlet while those of the sigmoid colon, adapted to the obliquely ascending lateral border of the intersigmoid recess, were attached at the inlet as well as more laterally.

Discussion

The dissections complemented the roentgenographic recordings by demonstrating the extent of the pampiniform plexus and the course of the ovarian artery at the level of point 2, the exact location of which could not be statistically determined by arteriography in non-pregnancy. In no respect did the results of

the two methods disagree each method complemented or confirmed the results of the other

The retroperitoneal space lateral to the para aortic section was thus symmetric. The abdominal relationships of the region, on the other hand, were asymmetric with regard to the topography as well as to the consistency and mobility of the structures. This asymmetry was not reflected in the course of the ovarian vessels or the ureter.

Dissection revealed that the three retroperitoneal structures examined were readily displaced by the application of direct or transmitted pressure or traction to the parietal or visceral peritoneum. They were for these reasons, indicators of forces applied to the posterior abdominal wall from the abdomen. The development of such forces in pregnancy is the subject of a later report (OHLSON to be published). The artificial displacement of retroperitoneal structures induced by dissection explains certain discrepancies between descriptions given by different authors as well as those between these descriptions and the results of the present investigation. For instance, in some of the drawings published by TESTUT & LATAUDET and PATURET which depict the ovarian vessels as passing the pelvic inlet 3 to 4 cm lateral to the ureter retractors can be seen pulling the caecum and the sigmoid colon laterally. BORELL & FERNSTROM compressed the aorta in some of their cases; the consequent lateral displacement of the ovarian artery appears in their roentgenograms. Where compression was not used the course of the artery confirmed the findings in the present investigation. The films of the two cases of DOS SANTOS reveal the extensive displacement of the artery caused by the greatly enlarged uterus. This is also apparent in certain cases in the series of FRATES. The asymmetric course of the ovarian artery above the inlet as depicted by PERKOFF is notable for its resemblance with the course of the artery in late pregnancy.

The configuration of the artery was consistently typical at arteriography as well as on dissection. All the characteristics were, in fact, present in a roentgenogram published by GESENIUS (1950) which represents part 2 as almost straight and part 3 as markedly tortuous, forming curves as well as axils and loops; the artery was hypertrophied on both sides. Hypertrophy was also present in certain arteries in the series presented by BORELL & FERNSTROM whereas in the present series no cases of hypertrophy were included. A statistical investigation of the artery in pregnancy indicated that hypertrophy involves widening of the artery proportional to the duration of pregnancy ($p < 0.01$) but with no significance for elongation; the characteristics of the configuration of the artery were preserved in all respects but one; the curves and loops were enlarged in proportion to the widening; hence to the duration of pregnancy (OHLSON to be published).

Before the roentgenographic demonstration of the ovarian artery the only report of its being tortuous was given by SOULIGOURX (1894) who described the vessel as forming convolutions. A drawing depicts the three kinds of distinctive figures although these are distributed equally over the whole artery. This is against the findings of the present investigation and was not encountered in pregnancy either. It is apparent that the contradictory findings reported earlier were due to technical circumstances that do not affect arteriography of the normal ovarian artery. In addition, the findings at dissection in the present investigation demonstrated that favourable technical circumstances may be obtained. Contradictions analogous to those mentioned apply to earlier reports of the configuration of the vein notably the extent of the pampiniform plexus. All drawings representing the artery as straight and surrounded by a plexus of communicating veins contain a striking resemblance between the tortuous configuration of the vein and the tortuous configuration of the artery found in the present investigation and the corresponding resemblance between the straight artery depicted and the straight vein found in the present investigation.

The tortuosity of part 3 and the mobility of the artery make it perfectly possible for the artery to reach both the medial and lateral aspects of the ureter as well as to cover both the common external and internal iliac arteries. The variability naturally becomes still more marked by the movements of the ureter and the topographic variations of the iliac vessels. These factors explain certain discrepancies in earlier reports of these structures.

The increase in tortuosity of the artery at the transition between parts 2 and 3 was not related to any other anatomic alteration in the artery, vein or ureter or of the tissue of the retroperitoneal space at this site. All cases in the present material were fertile or menopausal. The configuration of the artery before the menarche appears so far not to have been examined systematically. It is suggested that the cause of the characteristic configuration may be hormonal.

SUMMARY

The courses of the ovarian vessels and the ureter were investigated by arteriography and dissection and proved to be asymmetric in the para-aortic division of the retroperitoneal space but not lateral to that division. They reflected the state of symmetry of the abdominal wall in the non-pregnant state but not that of the intraabdominal organs. The vessels ran together in a caudal direction whereas the ureters converged.

ZUSAMMENFASSUNG

Die Verläufe der Ovarialgefäße und des Ureters wurden mittels Arteriographie und Dissection untersucht. Es zeigt sich, dass sie in der para-aortalen Teilung des retroperitonealen Raumes unsymmetrisch waren, jedoch nicht lateral an dieser Teilung. Sie spiegeln den Zustand der Symmetrie der abdominalen Wand im nichttrivialen Zustand aber nicht denjenigen der intraabdominalen Organe wider. Die Gefäße verliefen in einer kaudalen Richtung zusammen, während die Ureteren konvergierten.

RÉSUMÉ

Le trajet des vaisseaux ovariens et de l'uretère a été étudié par artériographie et par dissection et s'est révélé être asymétrique dans la division para-aortique de l'espace retro-péritonéal mais non pas latéralement à cette division. Ces trajets traduisent l'état de symétrie de la paroi abdominale en dehors de la grossesse mais non la symétrie des organes intra-abdominaux. Les vaisseaux se dirigent ensemble dans une direction caudale alors que les uretères convergent.

REFERENCES

- BORRILL U and FERNSTRÖM I. The ovarian artery. *Acta radiol* 42 (1954) 253
- CORNINO H K. *Lehrbuch der topographischen Anatomie* J F Bergmann München 1949
- CORNFORTHAM D J. *Text book of anatomy* Oxford University Press London 1938
- ELŠBA O. Venae et arteriae spermaticae a jejich variabilitě (In Czech) *Morfologie* 9 (1961) 200
- FRATTA R. Selective angiography of the ovarian artery. *Radiology* 92 (1969) 1014
- GRUNITS H. Arterienverschluss und ihre Beziehung zur Extremitätengangrän. *Zbl Gynak* 72 (1930) 257
- HARELIDGREN G and SCHILLING W. Die Bedeutung der Arteriae ovaricae für Postpartumbhungen insbesondere bei der Aortakompression. *Arch Gynak* 129 (1926) 300
- HUNTER W. *The anatomy of the human gravid uterus* London 1774
- *An anatomical description of the human gravid uterus* London 1794
- LEONARDO DA VINCI. I manoscritti di Leonardo da Vinci della Reale Biblioteca Windsor. *Dell'anatomia* Fogli A (In Italian) Edited by T Sabachnikoff and G Piumati Paris 1896
- *Quaderni d'anatomia* I-III (In Italian) Edited by O Vangersten A Fohlén and H Hopstock Jacob Dybwad Oslo 1911 and 1913
- MILROY F J, ANDERSON B J and CALDWELL E W. Variations in the inferior vena cava and their renal and lumbar communications. *Surg Gynec Obstet* 115 (1962) 131
- OHLSOY L. Coordinated topographic recordings in the abdomen. The ovarian artery as an indicator of the expansion of the uterus in pregnancy. *Acta radiol Diagn* 12 (1972) 705
- PATURET G. *Traité d'anatomie humaine* Tome III Masson et Cie Paris 1958
- PERKOWITZ E. *Atlas der topographischen und angewandten Anatomie des Menschen* Zweiter Band Urban & Schwarzenberg München Berlin 1964
- DELOS SANTOS R. Artériographie des membres et de l'abdomen. *Mémoires de l'Académie de Médecine* Paris 1931
- SOLLOUX CH. Artères et veines de l'utérus et de l'ovaire. *Bull Soc anat Paris* 63 (1894) 831
- TESTUT L et LATARET A. *Traité d'anatomie humaine* Tomes II-IV et V Doin et Cie Paris 1919

SUPRAILIAIC LYMPHOGRAPHY

J. BRUNA

KIMMORTH (1952) first described lymphography by the injection of contrast media directly into the lymphatic channels a method that has been widely applied clinically and proved useful (KIMMORTH 1952 RUTTIMANN 1965 FUCHS et coll 1969). Various types of lymphography have been introduced and lymphography of the foot and the arm have now been supplemented by cervical and intravisceral lymphography as well as lymphography of the penis and spermatic cord and the mesentery (WELLY & JOHANSSON 1968 FUCHS et coll 1969 MAJOTA & HLAUTHI 1969 DESPREZ CURELY & BISMUTH 1970).

This short communication describes a technique of suprailiac lymphography.

Method Two intracutaneous injections of 0.3 ml Parent Blue V 5% are injected 10 cm paravertebrally at the level of L4 on the two sides and demonstrate the group of lymphatics in the suprailiac region. After a local anaesthetic a longitudinal incision 2 to 3 cm in length is made in the region of the anterior iliac spine. Because the lymphatics in this area are in the order of 0.3 to 0.5 mm in diameter 40 to 100 mm needles (RUTTIMANN & DEL BOVO 1962) are used for the injection. About 5 to 6 ml Lipodol Ultrafluid are required for the demonstration of the lymph vessels and nodes of the pelvis and retroperitoneum the injection pressure should be 0.5 atm.



Fig. 1



Fig. 2



Fig. 3a



Fig. 3b

(For legends see opposite page.)

The roentgenography is carried out during and at 24 hours after injection of the contrast medium, films of the inguinal pelvic and abdominal regions as well as the chest being obtained in two projections

Discussion

The indication for suprailiac lymphography are the same as those for lymphography with injection of the contrast medium in the foot. It is valuable when the usual approach is impossible i.e. in lymphoedema of the foot and hypoplasia of the pedal lymphatics. The shorter distance from the regional lymph nodes makes the introduction of the contrast medium easier and decreases the time of the investigation: the application time is about 60 minutes. It is possible to demonstrate the pelvic (external and common iliac lymph nodes), retroperitoneal and lateral superior superficial lymph nodes.

The lymphatics of the suprailiac region are however generally smaller than those of the foot and the skin is also thicker than that on the dorsum pedis. The preparation of the lymphatics is therefore rather difficult. Successful suprailiac lymphography was performed in 6 cases; in a further 4 cases the lymphatics broke down during the procedure and in another 4 cases no suitable lymphatics were apparent.

Suprailiac lymphography cannot replace lymphography of the foot but it would appear to present a possible means of demonstrating the pelvic and retroperitoneal lymph nodes.

SUMMARY

Suprailiac lymphography has been performed successfully in 6 cases. It would appear to be suitable for the demonstration of the pelvic and retroperitoneal lymph systems especially when cannalisation of the lymphatics of the foot cannot be obtained.

ZUSAMMENFASSUNG

Die suprailiacale Lymphographie wurde erfolgreich in 6 Fällen ausgeführt. Diese scheint für die Darstellung des Lymphsystems des Beckens und des retroperitonealen Gebietes geeignet zu sein, besonders wenn eine Kanalisation der Lymphgefäße des Fußes nicht möglich ist.

Fig. 1. Suprailiac lymphography. Filling phase. Suprailiac and inguinal lymph channels outlined.

Fig. 2. Suprailiac lymphography. Filling phase. Suprailiac, inguinal and pelvic lymph channels as well as the superior inguinal and pelvic lymph nodes demonstrated.

Fig. 3. a) Combination of left suprailiac lymphography and lymphography of the right foot. Filling phase. The left suprailiac, inguinal and pelvic lymph channels are outlined. b) Storage phase. The right and left superior inguinal, pelvic and aortic lymph nodes filled.

Une lymphographie sus iliaque a été faite avec succès dans 6 cas. Cette méthode paraît convenir pour la mise en évidence des systèmes lymphatiques pélieux et rétropéritoneaux en particulier quand on ne peut pas réaliser une canalisation des lymphatiques du pied.

REFERENCES

- DESPREZ CURFELY J. P. et BRYNTH V. Deux ans de lymphographie. *Cah. méd.* 11 (1970) 1191.
- FLECH W. A., DAVIDSON J. W. and FRICHER H. W. *Lymphography in cancer*. Springer Verlag Berlin Heidelberg New York 1969.
- KYMNORTH J. B. Lymphangiography in man. *Clin. Sc.* 11 (1952) 13.
- MAKOTA N. and KIKUCHI T. Thyrodo-lymphography. *Radiology* 92 (1969) 359.
- RITTMANN A. Die Lymphographie. In: *Lehrbuch der Röntgendiagnostik*. Band I S. 413. Herausgegeben von H. R. Schinz, W. E. Baensch, W. Frommhold et coll. Georg Thieme Verlag Stuttgart 1965.
- WELLS S. and JOELANOW S. Lymphography. In: *Encyclopedia of medical radiology*. Vol VIII. Edited by L. Daethelm. Springer Verlag Berlin Heidelberg New York 1968.

RADIOGRAPHY OF THE LUMBAR INTERVERTEBRAL JOINTS

SVEN REICHMANN

Conventional radiography has been the only roentgen technique available for the examination of the lumbar intervertebral joints since the 1930s. The most detailed investigation of the method and its results were published by LANGE (1936). Its reliability was however questioned by HORWITZ & SMITH (1940) who observed such a large variability in the normal anatomy as to make it seem doubtful whether these joints could be examined at all by any standard means. These authors failed however to proceed any further on the question of reliability.

This communication is concerned with two kinds of roentgen examination. One consisted of conventional radiography with routine oblique projections, the other of fluoroscopic centering of each joint and subsequent film exposure.

Material and Methods

Ten lumbar spines were excised at autopsy. They were removed from 9 males and 1 female, aged from 21 to 42 years who had died suddenly. 88 joints were examined, pathological specimens being excluded. The spines were inserted

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into a special specimen holder where they could be rotated around their longitudinal axis

Standard projections A p and lateral projections were used in all specimens the central beam being directed 30 45 and 60° relative to the median plane from both sides. The joints of each side were thus depicted in four projections: the 0° projection (a p projection) the 30° projection the 45° projection and the 60° projection. The 90° projection (lateral) was unsuitable for the examination of the joints as symmetric structures were projected onto each other. This projection was used only for survey film of the whole spine.

Fluoroscopic centering Fluoroscopy was performed at 55 kV by means of a Philips Diagnost 70 with a TV unit containing a Plumbicon camera. Two projections were sought in each joint; in rare cases when the joint surfaces were unusually plane only one projection could be found. The two projections will be referred to as I and II. Projection I in each joint is the one with the largest incidental angle between the central roentgen beam and the sagittal plane.

Radiographic technique Non screen industrial film (CEA Test \ EL) was used the sensitivity of which is so low as to make possible $\times 3$ secondary magnification without disturbing graininess. The film was placed close to the specimen focus size 0.6 mm \times 0.6 mm FTD 75 cm, 90 kV. Tank development was used throughout.

Stereoscopic films were taken in the projections chosen by fluoroscopic centering; these being obtained by tilting the roentgen beam 5° so that it lay in the direction of the spine. Only angle films were taken in the standard projections. In addition to the registration in roentgen film the process of fluoroscopic centering was also fed into a Philips Medical Video Tape Recorder. Each joint was examined as the specimen was rotated from the lateral to the a p projection that is from the 90° to the 0° position. Every 5° during this rotation sequence was marked in the sound channel of the video tape. It was thus possible to re-evaluate the accuracy of the fluoroscopic process later when the spines had been macerated and the films inspected.

Evaluation of the roentgenograms These were compared with the skeletal specimens to decide whether a true representation of the anatomy had been obtained. The parts of the joints specially scrutinized were the joint surfaces and the capsular attachments. The stereoscopic films were examined in a mirror stereoscope at $\times 3$ magnification.

When the examination of 41 joints in 5 spines had still been uncompleted the question arose whether it was possible to judge from the remaining roentgen

Table

The number of joints properly depicted in the different projections

Projection	Number of joints	
	Right side	Left side
0	3	4
30	24	22
45	24	20
60	1	
I	30	4
II	14	17
30 + 45	34	31
I + II	34	39
Total number of joints	43	4

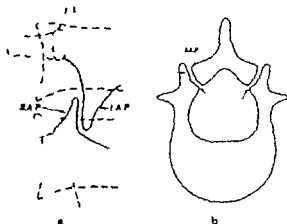
ograms alone whether the joints in question were reliably depicted or not. The author had by then become familiar with the roentgen anatomy from the examination of the other 47 joints of the material. This second half of the material contained 164 films.

The films and the joints of the whole material having been inspected, the fluoroscopic centering was re-evaluated as far as it was possible. The video recordings were re-examined and an attempt was made to establish anew the optimal projection angle for each joint. The projections earlier chosen were not known at this stage. An evaluation of the accuracy of this second fluoroscopic centering could be made only for the joints in which films had been obtained at an angle that did not deviate too much from the projection angle chosen at the second fluoroscopic inspection. This was possible in as many as 44 joints, many of the films of which had been originally taken for the examination of a joint in another segment of the spine.

Results

The value of each projection appears in the Table, which demonstrates the number of joints that were regarded as being accurately depicted in each projection. Owing to the curvature of the joint surfaces one joint could often be examined in several projections. It is evident that standard projections at 0° and 60° only rarely produced reliable roentgen images. It was therefore regarded desirable to see how many joints were properly depicted if only the 30° and 45° projections were used. It became clear that 65 joints could be

Fig 1 Main appearances of lumbar intervertebral joints. a) Ap projection of the joint on the right side. The articular processes of the joint between the two vertebrae are drawn in continuous lines. b) The two joints of one segment viewed from above and indicated by arrows within the spinal canal. The projection in (b) is perpendicular to that in (a) and is used in the drawings in Figs 2 to 5 to explain the final image with given direction of the roentgen beam. S A P is the superior articular process and I A P the inferior articular process.



acceptably represented by these two projections only. Likewise, 66 joints were accurately represented when the two projections chosen fluoroscopically were used together.

Many joints were not suitably reproduced by any projection in the different radiographic techniques. Nineteen of the 88 joints could not be reliably depicted in any of the four projections with the standard technique. Twenty-two joints could not be displayed by either of the two projections after fluoroscopic centering. 11 joints not acceptably demonstrated in any standard projection were well reproduced after fluoroscopic centering in at least one of the two projections. On the other hand 14 joints unsatisfactorily outlined in any projection after fluoroscopic centering could be demonstrated in at least one of the standard projections. Fluoroscopic centering thus failed to have any advantages over standard projections. This conclusion was not altered when the precision of the fluoroscopic centering was examined in a re-evaluation of 44 joints. The second fluoroscopic centering was regarded as successful in 30 of these joints and unsuccessful in 14 joints. Thus even detailed knowledge of the roentgen anatomy of the joints did not appreciably increase the reliability of the fluoroscopic centering.

The films were inspected before 5 of the spines were macerated in order to find out whether true and false appearances could be differentiated by means of the roentgen image alone. It was wrongly supposed in 26 of the 164 films that the conditions were satisfactory but in another 27 projections correctly assumed that good depiction was at hand. The remaining 111 films were regarded as unacceptable in the preliminary inspection. It was thus evident that

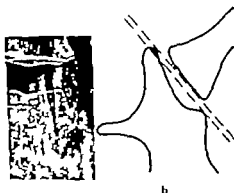


Fig 2 Incorrect depiction of intervertebral joint owing to overprojections from joint surface. In (b) the beam direction through the joint is demonstrated by interrupted lines which represent the ray forming the image of the joint space in the roentgenogram (). The joint space appears to be wedge shaped owing to overprojection from the interosseous margin of the superior articular process.

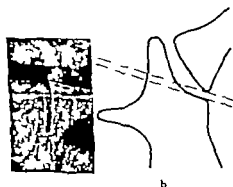


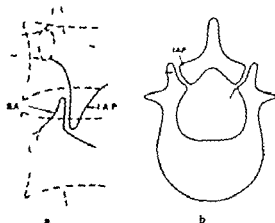
Fig 3 Incorrect depiction of intervertebral joint. The joint space in () is not formed by the joint surface proper of the inferior articular process (b) but by the capsular attachment which limits the joint space in the roentgenogram on the end of the inferior articular process. This cannot be concluded from the film.

not even a good knowledge of anatomy made it possible to judge from the stereoviews if the presentation was acceptable or not.

The main artefacts in radiography of the lumbar joints appear in Figs 2 to 6. The general appearances of a joint are illustrated in Fig 1. The roentgen beam in an oblique projection (Fig 1 a) used in examining the joints passes in a transversal plane through the body. Thus Fig 1 a corresponds to and explains the roentgenograms in Figs 2 to 6. In Fig 1 b the two joints in a segment appear from above in a projection perpendicular to the one in Fig 1 a. This aspect of the joints is presented in the drawings of Figs 2 to 5; they demonstrate what was evident in the anatomic specimens as to the development of the final roentgenogram. The drawing in Fig 6 b depicts the joint in the same projection as the roentgenogram in Fig 6 a.

The curvature of the joint surfaces in the transversal plane caused most of the difficulties in interpretation. The joint surface of the superior articular process was especially difficult to depict in a reliable way. A common form of

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Fig 5 Incorrect widening of the joint space. Separate parts of the joint surfaces are struck by tangential roentgen rays (interrupted lines) (b). An apparently widened joint space is thus recorded (a) to suggest retro-olisthesis back and gliding of the upper vertebra.



Fig 6 Incorrect depiction of the apical attachment. The drawing (b) demonstrates the joint in the same projection as the roentgenogram (a). The joint surface proper in this projection ceases at the arrow (b); the lower part of the inferior process being situated more anteriorly in the joint. The film fails to demonstrate that the projected joint surface is not representative of the whole of the true joint space.

The joints in Figs 2 and 3 had an inferior articular process surface that was slightly but definitely curved. A joint in which this surface was plane appears in Fig 4 a. Such a joint is hard to demonstrate since only one projection is satisfactory for the registration of the plane joint surface. When the projection was the one indicated in Fig 4 b no satisfactory representation of the superior articular process was possible, the joint surface of this process being superimposed on the laminary process. In Fig 4 a this process is projected onto the joint space making investigation of the joint impossible. When the projection was adjusted so as to render good demonstration of the superior articular process (Fig 4 d) the inferior articular process was not struck tangentially by the roentgen rays. Consequently a double contour of the inferior articular process appeared in the roentgenogram (Fig 4 c). Thus the greater the incongruity between the joint surfaces the more difficult was it to obtain proper demonstration. The difficulty was maximal when the joint surface of the inferior articular process was plane.

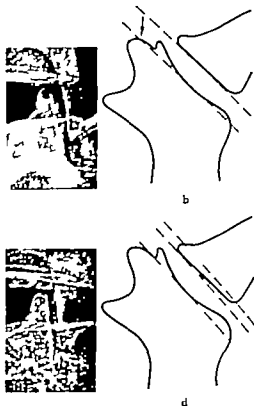


Fig 4 Plane joint surface of the inferior articular process (Cf b and d where the joint is seen from above.) When this surface is struck tangentially by the rays (interrupted lines) the joint surface of the superior process is concealed by an overprojecting mamillary process (indicated by arrow in b) so that the joint cannot be examined (c). If the projection be adjusted to eliminate the overprojection the surface of the inferior process will not be struck tangentially (d) resulting in double contour in the roentgenogram (e).

artefact appears in Fig 2 the roentgen rays passed along the joint surface of the inferior process and was accurately depicted. The contour of the superior articular process however did not stem from the joint surface proper but from its anteromedial margin which was not parallel with the joint surface of the inferior process the resultant joint space form being spuriously wedge shaped in the roentgenogram (Fig 2).

The osseous parts of the joint surfaces of one lumbar joint were seldom congruous. The curvature of the joint surface of the superior process was usually more marked than that of the inferior process (Fig 3 b). The joint appeared to be well demonstrated (Fig 3 a) but as is evident from Fig 3 b the joint surface contour of the inferior articular process in these cases may be derived from the anteromedial margin of the joint surface this was not regarded as a good depiction of the joint. It was often noted that if the projection was changed so that the roentgen rays passed along the joint surface of the inferior process false depiction of the type demonstrated in Fig 2 was obtained.



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Fig 6 Incorrect depiction of the capsula attachment. The drawing (b) demonstrates the joint in the same projection as the roentgenogram (). The joint surface proper in this projection causes () the arrow (b) the lower part of the inferior process being situated more anteriorly in the joint. The films fail to demonstrate that the projected joint surface is not representative of the whole of the true joint space.

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The errors in depiction mentioned usually gave rise to a false impression of a reduction in the joint space width. However, it was also evident that spurious widenings of the joint space could appear (Fig 5). This was encountered in joints with a special form of incongruity between the osseous joint surfaces. The form of the osseous joint surface of the inferior articular process might be concave in the transversal plane instead of plane or convex, as is usual (Fig 5 b). A projection might be evident where the joint space in the film was derived from different parts of the joint, the resulting effect being a remarkably wide joint space.

Errors in representation were also encountered in the capsular attachments: the most common of these appears in Fig 6. What seems to be a true joint space in Fig 6 a proved to be a joint space proper only in the region above the arrow in Fig 6 b. The roentgen rays passed along the most posterior parts of the joint surfaces: the longitudinal extensions of the joint surfaces in this region were less than in the middle of the joint. The part of the inferior articular process indicated below the arrow in Fig 6 b was actually seen in this central region of the joint at a distance from the true joint surface part depicted of about 1 cm in the beam direction. The joint space of the roentgen image thus had a larger longitudinal extension than the joint surface in the corresponding region of the joint. The capsular attachment of the inferior articular process was situated in a part of the joint other than that of the surface part depicted. Such representation was considered unsatisfactory.

Discussion

The joint surface anatomy of the lumbar intervertebral joints makes them unsuitable for conventional radiography. Two matters contribute to this fact: the incongruity between the osseous parts of the joint surfaces in one and the same joint, and the great variations in the joint surface anatomy when different joints are compared. This investigation has demonstrated that an increasing number of projections will lead to increasing chances of good representations of the joints. However, the films cannot indicate whether these are accurate or not. Even with many projections there will still be a considerable amount of false information about the joints that cannot be recognized as misleading. This infers that conventional radiography is of little value in the examination of these joints. The same conclusion is valid for conventional radiography after fluoroscopic centering of each single joint. Stereoscopic views failed to provide more accurate information than single films. REICHMANN (1972) has demonstrated that the lumbar joints may be accurately examined by means of wide angle tomography with a multidirectional movement, preferably hypocycloid. It

should be stated that if these joints are to be examined this type of tomography should be used without prior conventional radiography.

Little is known about the clinical importance of the lumbar intervertebral joints. Autopsies have demonstrated that pathologic changes are not infrequent (GURTZ 1933/34, LEWIN 1964). However, virtually all that has been said about the clinical signs arising from such pathologic states in the joints has been based upon radiologic examinations in which only conventional radiography was used. It would appear that all these investigations have been based on an unsatisfactory roentgen method.

An examination of the joint surfaces of different lumbar joints discloses considerable variations in form and orientation. Such variations may be encountered in one single segment, i.e. the two joints of one segment may be asymmetric. Joint surface asymmetry has been presumed to lead to an early and intense development of osteoarthritis (PUTTI 1927, PHEASANT & SWENSON 1942). Some authors have described asymmetries in a conventional roentgenogram as if these could be demonstrated from two oblique projections of the segment (KUHNS 1935, BADOLEY 1941, BORMAN 1959). The problem is however rather more involved. PHEASANT & SWENSON in comparing conventional films with the anatomy decided that one projection of each joint was insufficient for the demonstration of asymmetries. This was confirmed by the present investigation. In fact it became evident that asymmetries may not always be demonstrable even if many projections be taken since a false joint space may be produced in those in which the surfaces are not struck tangentially by the beam (Fig. 3). Fluoroscopy in different projections could also not be used for the demonstration which appeared theoretically to demand transversal tomography. It is however doubtful whether even the precision of this method would be sufficient. It would thus appear that no satisfactory solution has been encountered up to the present time.

SUMMARY

The lumbar intervertebral joints from ten spines excised at autopsy were examined by means of conventional radiography in standard projections and in others selected by TV fluoroscopy. The films were compared with the anatomic specimens. Conventional radiography proved to be totally unsuitable for the examination and fluoroscopic centering and stereoradiography failed to increase reliability. Certain aspects of the joint surface anatomy appeared to be the main causes for the failure of conventional radiography.

ZUSAMMENFASSUNG

Die lumbalen Intervertebralgelenke von zehn bei der Autopsie herausgehobenen Wirbelsäulen wurden mit Hilfe konventioneller Röntgenuntersuchung in Standardprojektionen und in solchen, die durch Fernsehdurchleuchtung ausgewählt waren, untersucht. Die Filme

wurden mit den anatomischen Befunden verglichen. Konventionelle Röntgenuntersuchung erwies sich als vollständig ungeeignet und Zentrierung bei Durchleuchtung und Stereoröntgenuntersuchungen ermöglichten die Zuverlässigkeit nicht zu erhöhen. Gewisse Eigenheiten der Gelenkflächenanatomie scheinen die wesentlichen Ursachen für das Versagen der konventionellen Röntgenuntersuchung zu sein.

RÉSUMÉ

Les articulations intervertébrales lombaires de dix colonnes prélevées à l'autopsie ont été examinées par la radiographie simple dans les projections standards et dans des projections choisies par radioscopie. Les films ont été comparés avec les pièces anatomiques. La radiographie simple s'est montrée totalement insuffisante pour l'examen, et le centrage radioscopique et la stéréoradiographie n'ont pas augmenté la fidélité de cet examen. Certaines particularités de l'anatomie de la surface articulaire semblent être la principale cause d'échec de la radiographie simple.

REFERENCES

- BADLEY C. The articular facets in relation to low back pain and sciatic radiation. *J. Bone Jt. Surg.* 23 (1941): 481.
- BORMAN R. H. Lumbosacral zygapophysial tropism and the radiculodisk syndrome. *J. Amer. osteopath. Ass.* 58 (1959): 755.
- GUNTZ E. Die Erkrankungen der Zwischenwirbelsäule. *Arch. orthop. Unfall-Chir.* 34 (1933/34): 333.
- HORWITZ T. and SMITH R. M. An anatomical, pathological and roentgenological study of the intervertebral joints of the lumbar spine and of the sacroiliac joint. *Amer. J. Roentgenol.* 43 (1940): 173.
- KRINS J. G. Developmental changes in the vertebral articular facets. *Radiology* (1935): 498.
- LANGER H. Die Wirbelgelenke. Ferdinand Enke Verlag Stuttgart 1936.
- LARSEN T. Osteoarthritis in lumbar synovial joints. *Acta orthop. scand.* (1964) Suppl. N. 73.
- PRESTANT H. C. and SYMONSON I. C. The lumbosacral region. A correlation of the roentgenographic and anatomical observations. *J. Bone Jt. Surg.* 24 (1942): 299.
- PUTTI A. New conceptions in the pathogenesis of sciatic pain. *Lancet* II (1927): 30.
- REICHMANN S. Tomography of the lumbar intervertebral joints. *Acta radiol. Diagn.* 12 (1972): 641.

PRECOCIOUS TYPE OF OSTEODYSPLASIA

A new autosomal recessive form

K. KOZŁOWSKI, V. MAYNE and D. M. DANKS

Bone dysplasia resembling the osteodysplasia described by MELNICK & NEEDLES (1966) and MAROTRAUX *et coll.* (1968) was encountered in three babies all of whom died from two families. It was however more severe and probably inherited as an autosomal recessive trait.

Case reports

Case 1 Female infant aged 9 months admitted with pneumonia. She was the first child of healthy parents (father aged 33 and mother 38). She weighed 2.03 kg at birth after normal pregnancy and delivery weight on admission 4.7 kg. She had had repeated upper respiratory tract infection.

The extremities especially the hands and feet were short and the finger nails and toe nails small. The trunk was relatively long with the head normal. Routine laboratory tests including serum calcium, phosphate and alkaline phosphatase estimations were negative, no increase in mucopolysaccharide excretion in the urine. ECG revealed right ventricular hypertrophy. The child subsequently died from further pneumonia.

Case 2 Male infant aged 4 weeks born in Melbourne to unrelated Albanian parents but both from the same village of 500 inhabitants. The pregnancy was the 31 year-old mother



Fig 1



Fig 2

Fig 1 Case 2 at 11 weeks. Lower limb. Poor moulding of the diaphyses.

Fig 2 Case 3 at 11 weeks. Upper limb and hand. Abnormal shape of long bones, shortening of radius and ulna.

fourth and was uneventful. The three older children (2 females, 1 male) were normal, no drugs were taken and no viral infections were apparent. Rapid breech delivery at 39 weeks, the child weighing 2.27 kg. The length was not recorded at birth, but was 41 cm at 4 weeks on admission with complaints about his feeding.

The face was round with plentiful dark hair extending down on to the forehead. The trunk was normal, but the limbs were short and the hands especially small. The fingers were minute, little bone was palpable and the nails were mostly absent. Urography revealed bilateral dilatation of the ureters without vesico-ureteric reflux during micturition cysto-urethrography.

Feeding difficulties remained a problem and the child developed poorly, weighing only 3.5 kg at 6 months and measuring 45 cm at 5 months. Mental development probably within normal limits. The baby died at the age of 9 months.

Case 3. Female infant born in Melbourne was the younger sister of Case 2. Fifth and normal pregnancy with weight at birth 2.52 kg and limb malformations identical to those in the brother. Broad face with ears low set and prominent ulnar deviation of the short hands with feet dorsiflexed and everted. Pulmonary infections necessitated three admissions during the 11 months she lived. She grew to only 3.73 kg and from 41 cm at birth to only



Fig 3 Case 3 t 1 week Foot. Short poorly moulded metatarsal bones absence of ossification of some phalanges

46 cm at 9 months the head enlarged from 34 cm at birth t 43.5 cm at 9 months and the anterior fontanelle remained widely open

The bone changes were generalised but varied in roentgenographic diagnostic value the long bones of the extremities and the small bones of the hands and feet (Figs 1 2 3) presenting striking disturbances in bone modelling and ossification The shafts of the long bones were broad and failed to have the normal gradual widening towards the metaphyses The ends of some bones tapered and others presented abrupt metaphyseal widening from a localised submetaphyseal narrowing while many had a rectangular shape Diaphyseal indentation and irregularity of the cortex was present in the proximal ends of the femora and radii Some proximal shortening of the radius and ulna was also evident The metacarpal and metatarsal bones were shortened and poorly shaped and many phalanges in the two younger patients (Cases 2 3) were poorly ossified with the bone age much retarded in all three patients (Figs 2 3)

Less marked although definite changes were present in the pelvis thorax (Fig 4) and vertebral column The iliac angles of the pelvis were decreased and the iliac crests flared The supra iliac regions in Case 1 were narrow Coxa valga was present in all three The ribs were slender and irregular in



Fig. 1



Fig. 2

Fig. 1 Case 2. At 11 weeks. Lower limb. Poor moulding of the diaphyses.

Fig. 2 Case 3. At 1 week. Upper limb and hand. Abnormal shape of long bones, shortening of radius and ulna.

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Discussion

It would appear that no similar cases have been reported in the literature. The radiographic changes in these 3 infants bear some resemblance to those in the 7 month-old baby described by MAROTEAUX *et coll*. However, this baby was quite healthy and his mother clearly had the same condition which the authors termed osteodysplastic. They pointed out that the patients suffered from the same condition as the 12 patients from two families described by MELNICK & NEEDLES. The inheritance in these previous reports was clearly autosomal dominant. Although a resemblance to osteodysplasia is quite definite, the present 3 babies differ greatly in their poor growth and health which ended in their early death; the radiographic changes were also much more marked. All three were born to normal parents.

There would appear to be two forms of osteodysplasia: a precocious one represented by the present cases and a late one as described by MELNICK & NEEDLES and MAROTEAUX *et coll*. The inheritance, radiographic changes and the clinical course indicate that these are perhaps different entities. The existence of severe recessively inherited and less marked dominantly inherited forms of bone dysplasia is well known, e.g. in osteopetrosis.

Future investigations of children with this precocious form of osteodysplasia should include detailed investigation of immune mechanisms. The bony defects in these three cases fail to provide an adequate explanation for the deaths or the failure to thrive or for the susceptibility to respiratory infection. Unfortunately no autopsies were performed in these cases.

SUMMARY

Three babies from two families with generalized bone dysplasia resembling cases described by MELNICK & NEEDLES (1966) and MAROTEAUX *et coll* (1968) but with more marked roentgen changes and a clinical course leading to death and with autosomal recessive inheritance are described. It is suggested that this condition be termed the precocious type of osteodysplasia.

ZUSAMMENFASSUNG

Drei Säuglinge von zwei Familien mit generalisierter Knochen dysplasie werden beschrieben. Diese sind den von MELNICK & NEEDLES (1966) und MAROTEAUX *et coll* (1968) beschriebenen Fällen ähnlich, haben jedoch stärker ausgeprägte roentgenologische Veränderungen, einen klinischen Verlauf, der zum Tod führt und einen autosomalen, rezessiven Erbgang. Es wird vorgeschlagen, diesen Zustand als frühreifen Typ der Osteodysplasie zu bezeichnen.

RÉSUMÉ

Les auteurs présentent les cas de trois bébés de deux familles atteints d' dysplasie osseuse généralisée ressemblant aux cas décrits par MELNICK & NEEDLES (1966) et par MAROTEAUX et coll (1968) dans leurs cas les signes radiologiques étaient beaucoup plus marqués l'évolution clinique a conduit à la mort et l'un avait une hérédité récessive autosomique. Les auteurs pensent que cette affection peut être appelée le type précoce d'ostéodysplasie.

REFERENCES

- MAROTEAUX P, CHOLRAKI L et COSTE P. L'ostéodysplasie. Syndrome de Melnick et de Needles. *Presse med* 76 (1968) 715.
- MELNICK J. C and NEEDLES C. F. An undiagnosed bone dysplasia. A two family study of four generations and three generations. *Amer J Roentgenol* 97 (1966) 39.

IMPORTANT SOURCES OF ARTEFACTS IN MULTICOLOR ANGIOGRAPHIC COMBINATION IMAGES

B SCHIAPPI and U WELANDER

Two or more roentgen images may be combined by means of color processing. If the different component views in serial angiography for instance be subtracted and then given suitable colors and combined the differences between the views will appear as changes in hue. The combination of suitable phases in serial angiography may produce information of diagnostic value both as regards the anatomy and the circulation (LILJEQUIST & WELANDER 1969, 1970; WELANDER 1969).

The color films in the original presentation of the method were prepared with Kodachrome developers. The Kodachrome method is both complicated and time consuming however and a simplified technique already mentioned briefly in the original publication has since been worked out for use in routine work (EKLUND *et alii* 1973). This new method is based on the diazo-type process which permits the production of positive color prints within a few minutes. The diazo films are exposed with the aid of ultra violet light and are developed in ammonia fumes. The developing is carried out in the dry state, and the developed film requires no after treatment in the form of fixation or other measures.

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The purpose of the multicolor angiographic combination image is to demonstrate visually the differences between two or several phases of a serial angiography. The differences between the component views may best be observed if the changes in hue appearing when the components are combined are optimal and not disturbed by inappropriate color variations. Factors that produce artefacts in multicolor combination images have been touched upon only briefly in earlier publications. Various types of artefacts that may lead to misinterpretation of the information in the image are however already present in the original black and white films. Optical illusions as well as psychologic factors always play a part in making the interpretation of roentgen images difficult. Further sources of error are added when a number of separate images are unified into one composite image and color is introduced. Technical errors may occur during the preparation of masking films for subtraction, subtraction images as well as the color images. The end result is also influenced by the properties of the material used for the color films. Finally, psychophysiologic phenomena connected with the ability to perceive and assess color sensations may also arise when the color image is being interpreted.

The aim of this paper is to describe the more important artefacts arising in the preparation and interpretation of multicolor combination images and to analyze their causes.

The combination image

A technically satisfactory multicolor combination image together with the black and white subtraction images of which it is composed appears in Fig. 1. Like the subtraction images, the combination image is also a positive. The blood vessels appear in a continuously changing color scheme against a neutral background that represents weak density of the skull bones. The original black and white subtraction images are equal as regards density and contrast and in the multicolor combination image the corresponding properties of the three monochromatic color images are also alike: neither one nor the other of the component views dominates the others.

Diagnostically valuable differences between the component views may be assessed by observing the color shifts in the combination image caused by the successive movement of the contrast medium between the exposures. The method may be described as an advanced form of tracing in which several images may be superimposed without cancellation of the information in the individual component views.

The assessment of the multicolor combination image, which has been analyzed thoroughly in an earlier publication (WELANDER) is based on the following principle. Details present in only one of the original component views will appear in the combination image in the color belonging to that view and details evident in two of the component views or in all three will appear in compound colors. Maximum color shifts will be obtained if each of the component views be given one of the subtractive primary colors yellow, magenta, and blue green (cyan). When yellow and magenta are combined the resultant color will be red and a combination of magenta and cyan gives blue; the three colors in combination result in gray or black if they all have the same density and in various brownish shades if they are unequal in this respect. This phenomenon makes it possible to examine in one image relative differences in the speed of the circulation through the different vessels.

Geometric errors. A roentgen image is a two-dimensional projection of a three dimensional object. When the relative speed of the circulation through different blood vessels is assessed with an angiographic technique this may mean that circulatory differences are simulated because of the differing direction of the vessels in relation to the film plane. The circulation seems to be more rapid in a vessel running parallel to the film plane than in one that forms an angle with it. In rapid serial angiography the circulation may for a brief moment appear to be stationary in a vessel that forms a right angle with the film plane. This factor however is probably of minor significance in the assessment of serial angiograms if consideration be paid to anatomic knowledge regarding the length of the vessel segments that form a sharp angle with the film plane.

The geometric errors are already inherent in the black and white original films, and the purpose of the multicolor combination image is to facilitate the interpretation of any differences existing between them. The risk of misinterpreting the color image because of geometric errors is no greater than that of misinterpreting the original films.

Incomplete representation of details. In connection with the processing of the original films through subtraction films to monochromatic color images the possibility exists that individual details in the original films, especially those of low density, will be lost. If loss of detail has occurred in one component view — or in two but not in the third — colors that are not relevant for diagnosis will appear in the combination image.

To avoid such artefacts the technical procedure for the printing work should be optimal. The subtraction of the skeleton must not be absolutely complete; should the skeleton appear with a homogeneous density both in the sub-



FIG. 1. A multi-color combination image of satisfactory technical quality. The subtracted skeletal structures are depicted in neutral gray and the vessels appear in continuously changing color scheme. The circulation in case of congenital steno-venous malformation.

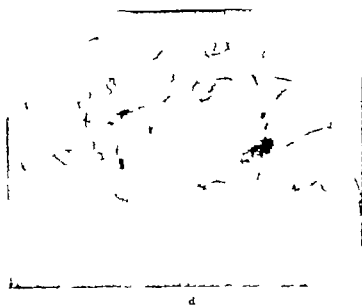
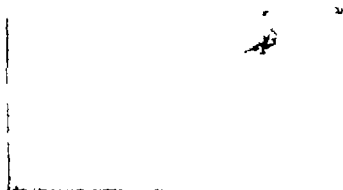




Fig. General color bias the second magenta colored component now is the dominating color

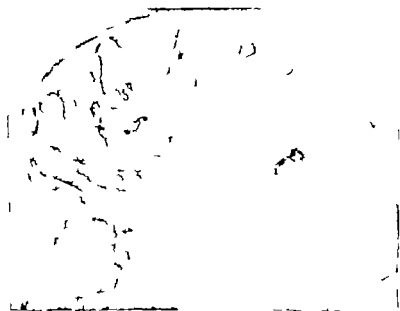


Fig. 3 L. color bias the high contrast colored component now has been subtracted the masking film which had contrast was too high



Fig. 4 Outline relief and grid interference resulting from displacement between the component views

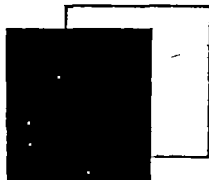


Fig. 5 Representation of approximate color constancy. The yellow line is interpreted as yellow even in those areas where it passes through magenta and cyan field. Objectively the line is reddish and greenish respectively in these areas.

traction films and the monochromatic color films then all details of the blood vessels will have been carried over from the original films to the color images (Fig 1 a b c)

General color bias Unbalanced color in a color combination image means that the former is not of equal density in the monochromatic component views with the result that one or two, of these views will dominate or be suppressed. When a multicolor combination image is out of balance in this way the background — the skeleton — will not be depicted in neutral gray but will instead appear in color (Fig 2). If one of the component films has higher density in comparison with the others the color of that film will dominate, and if two of the components have too high density in relation to the third the compound color of these two will dominate. If one of the component films is of too low density the complementary color, i.e. the combined color of the other two films, will be over emphasized in the combination image. Unbalance of color may be observed best in the shadows of the subtracted skeletal structures in the color image, but naturally it is also present in the representation of the blood vessels.

If the unbalanced color is uniform all over the image the cause, as mentioned above, is difference in density between the monochromatic component films due either to errors during the printing of the color films or to density differences between the original black and white films. In order to avoid imbalance it is essential that the original films, the masking films, the subtraction films, as well as the color images have the same degree of background density.

It is almost impossible completely to avoid color bias in the preparation of combination images. However a moderate amount of imbalance is of little significance when the films are being viewed since the ability of the eye for adaptation in the interpretation of color sensations is considerable. The light that illuminates a colored object or the viewing light during the examination of a color image appears neutral within a wide tolerance range. This phenomenon is usually known as general color adaptation and such adaptation should make it possible to grade correctly the relation between different hues when seen against a relatively uniform background. Another factor inherent in the faculty of vision, known as color constancy, also acts in the same direction. This is the ability to experience a color as correctly irrespective of the color of the viewing light. For instance, a yellow object seen under blue light or viewed through a blue filter will give a different color impression but subjectively the color is still experienced as yellow (Fig 5).

Local color bias Unbalanced color may arise in the color image not only through differences in density but also because of contrast differences between the original films and the color prepared component films. With contrast dif-

ferences however the imbalance is not uniformly distributed over the whole image (Fig. 3). If the contrast in one of the component films is higher than in the others the color belonging to that component will dominate in the areas with high density but will be under emphasized in those of low density.

Differences in contrast between the component views of the combination image tend to occur during the preparation of the subtraction films. This is mainly because of the contrast properties in the masking films. To avoid local color bias the subtractions of all the component films should if possible be carried out with the same masking film and in any event the masking films must be exposed and developed in identically the same way.

Moderate local unbalanced color need not necessarily affect the interpretation of the multicolor combination image. Here again, the ability of the eye for adaptation in relation to the background — approximate color constancy — plays a part (Fig. 3). It should however be borne in mind that objective color changes in the blood vessels may be due to a shift in the color of the background. Such an alteration in background color may be due to an artefact, but may also arise as a result of physiologic factors such as a normal or abnormal concentration of contrast medium in the capillaries.

Different degrees of color bias occur to a greater or lesser extent in all combination images. Objectively speaking the colors will thus vary in different combination images and consequently direct comparisons cannot be made between them. This is not the purpose of the image combination however the object is merely to demonstrate the differences between the component views that have been combined.

Shifts in hue. When the colored component views are combined into a combination image optimal color shifts will arise in individual details only when the component films have identical density. A pure red color for instance appears only when the yellow and magenta films are of the same density and a pure blue color only when the magenta and cyan films are of equal density.

Difference in density from one component film to another is always evident in vessel segments depicted in serial angiography due to variations in the dilution of the contrast medium with blood. The concentration of the contrast medium varies during the circulation, and at the beginning and end of the contrast column there is considerable dilution with blood, with the result that the vessel in those areas are depicted in the subtraction film with a lower degree of density. This is represented as changes in color in the combination image and may cause difficulties of interpretation.

Differences in shades between adjoining hues should be assessed with caution when it is a question of the circulation in blood vessels. The entire scale of red

colors from orange to red mauve denotes that the detail under investigation is present in both the yellow and magenta component films similarly all blue colors from blue mauve to blue green denote that a given detail is present in both the magenta and cyan component views. However the relative color difference between various red or blue tones is not always relevant when the circulation is being assessed owing to true or incorrectly represented differences in density between the component films.

Brown tones Any detail present in all three component views comes out in the combination image in gray or black in the ideal case. For this to occur however this particular detail must have the same degree of color saturation in all three component films. If this is not the case, the detail will be depicted in different shades of brown. Brownish colors are thus to be expected when a multicolor combination image is to be interpreted, and their implication is that the detail in question is present in all three component views.

Green tones With the colors chosen for the three component views — the first in yellow, the second in magenta, and the third in cyan — the blood vessels are depicted in one of the following color schemes: yellow-magenta-cyan, yellow-red-magenta-blue-cyan, or yellow-red-black (brown)-blue-cyan. A vessel can only appear in green if it contains contrast medium in the first yellow and the third, cyan component view but not in the second magenta view. If this phenomenon be physiologically possible the green color is of interest in the interpretation of the combination image but otherwise green is an artefact that has arisen in connection with the preparation of the color picture and signifies that the information contained in the second component view has been suppressed in the combined view.

By combining color images schematically in a suitable way (EKLUND *et al*), it is possible to investigate the color changes optimal or non optimal that occur when two or three component views are combined. A reference model for the assessment of the multicolor combination image may also be obtained by preparing a schedule of the possible color combinations on the basis of the process used.

Outline relief grid interference All differences between the component views are depicted in the multicolor combination image and the original views are therefore represent exactly the same projection. Those details that are common to all the views and that have the same density will coincide completely in the component views are superimposed and they will have a uniform relief in the combination image. Details that are not common to all the views will appear on the other hand have another color in the combination image determined by the component views in which the detail in question is represented.

A very slight difference in projection between the component views forming a combination image is tolerable, but if it is of such magnitude that a black and white subtraction can be prepared only with difficulty it will be hard or even impossible to obtain an assessable color image. Even very small differences in projection between the views will result in the outlines of all the details in the combination image appearing in multicolored relief (Fig. 4).

As a stationary grid is used during serial angiographies even very small differences in projection will result in different grid orientation between the films. When three views with deviating orientation of the grid lines are combined, disturbing interference phenomena will cause difficulties in the interpretation of the combination image (Fig. 4).

Owing to the effects of these two phenomena multicolor combination images can only be obtained if the patient is satisfactorily immobilized during the examination.

Discussion

Photographic processes are always subject to artefact producing sources of error both technical errors which affect the properties of the image, and those of a psychophysiologic nature which influence its interpretation. In the technical preparation of multicolor combination images there are several factors that must be under control if the final product is to have optimal qualitative properties. The psychophysiologic phenomena that arise during the analysis of the image cannot however be fully controlled.

The faculty of vision is highly complicated and the individual ability to perceive color sensations varies widely with total color blindness as an extreme example. A thorough knowledge of the theoretic aspects of the color image and of color mixtures is a prerequisite for adequate interpretation of the colors in a multicolor combination image. The ability to perceive colors and differences in color is furthermore largely a matter of training; this factor works in the same way as the ability to observe diagnostically relevant density differences in a conventional roentgen image.

The multicolor combination image contains no information that is not already present in the original films. The use of color films however if applied adequately facilitates the assessment of the original images through the fact that differences in the distribution of the contrast medium between these films are depicted as changes in color. If attention has been drawn to a particular detail with the aid of the color image this detail must also be verifiable in the original films. A possibility is thus provided to check the information in the color image and thereby avoid misinterpretation due to artefacts.

Appendix

The illustrations in this article were produced by a simplified method for preparing plates for multicolor combination images devised by PARRMAN & WELANDER

SUMMARY

A brief description is given of a method of applying color films in roentgenology by the use of multicolor images. Following an analysis of the properties of a qualitatively satisfactory combination image factors that may give rise to artifacts in its preparation are considered. The effect of such causes and the possibilities of eliminating them are also discussed.

ZUSAMMENFASSUNG

Es wird eine kurze Beschreibung von einer Method Farbfilm in der Röntgenologie durch Verwendung von Mehrfarbbildern anzuwenden gegeben. Im Anschluss an eine Analyse der Eigenschaften eines qualitativ zufriedenstellenden Kombinationsbildes werden die Faktoren die bei der Herstellung Anlass zu Artefakten geben können betrachtet. Die Folge von solchen Artefakten und die Möglichkeiten diese zu eliminieren werden ebenfalls besprochen.

RÉSUMÉ

Bref description d'une méthode d'utilisation de films en couleur en radiologie au moyen d'images multicolores. Après une analyse des propriétés d'une combinaison d'image qualitativement satisfaisante les auteurs étudient les facteurs qui peuvent donner lieu des possibilités de les éliminer.

REFERENCES

- EKLUND S, JEWBRATT L, SCHAMPI B and WELANDER U. The diapo method. A simplified method of preparing multicolor combination images for use in roentgen diagnosis. *Acta radiol. Diagnost.* 14 (1973) 33.
- LELIGERST B and WELANDER U. Colour in subtraction angiography. Preliminary report. *Acta radiol. Diagnost.* 8 (1969) 1.
- — Colour combination images in cerebral angiography. *Neuroradiology* 1 (1970) 39.
- PARRMAN H J and WELANDER U. Printing of multicolor combination images intended for roentgenologic application. To be published in *Acta radiol. Diagnost.* 14 (1973).
- WELANDER U. Multicolor combination images in subtraction angiography. A new photographic method and its applications. *Acta radiol.* (1969) Suppl. No. 290.

THROMBOGENIC PROPERTIES OF VASCULAR CATHETER MATERIALS IN VIVO

The differences between materials

D SCHLOSSMAN

Thrombo-embolism following catheterization of blood vessels appears to be due mainly to the formation of thrombi on the catheter (JACOBSSON & SCHLOSSMAN 1963). It is however not known whether such thrombus formation varies with the composition of the catheter material. This may perhaps be explained largely by the absence of a suitable method for comparing thrombotic properties.

SCHLOSSMAN (1973) regarded thrombotic properties of a given material as their tendency to *initiate* thrombus formation. He also described a device for simultaneous formation of thrombi on various catheter materials in vivo. Experiments with this device reflected the degree of early thrombus formation particularly as judged from the amount of labelled platelets in the thrombi. Since adhesion and aggregation of platelets are the first steps in the formation of a thrombus it was considered justified to regard the amount of platelets in freshly formed thrombi on the catheter as a good measure of the thrombotic properties of the actual product examined.



POSITIONS OF pieces of catheter materials in control and test devices. In the control device all compartments consist of polyethylene and in the test device of polyethylene (left) polyethylene with lead oxide (middle) and teflon (right)

The purpose of the present investigation was to determine whether and how differences in the thrombogenic properties of various compounds could be demonstrated. It consisted of three series. The object of series I and II was to find out whether experiments in venous or arterial flow were more informative and to arrive at a suitable duration of exposure of the substances to the blood stream for demonstrating differences in their thrombogenic properties. The results in these first two series formed the basis for the experiments in series III for deciding how the method should be used for testing materials. The result in this series reflected also the thrombogenic properties of the products.

Material and Method

The device. The device used for producing simultaneous thrombus formation on pieces of catheters of different substances has been described in detail in a previous article (SARLOSSEMAN). It was made up of three pieces of catheters of optional materials and could be inserted in the aorta or the inferior vena cava or both by transfemoral catheterization. The pieces were of equal dimensions and had the same number of side holes distributed in exactly the same way; these holes permitted the flow of blood through the pieces and thereby the formation of thrombi on their inner surfaces so that after withdrawal of the device the thrombi on the respective specimens could be examined and compared.

The device consisted of pieces of the same catheter material in each of the experimental series as described in the previous report; it will be referred to as the test device.

The sequence of the pieces in the test device was regularly varied in series I and II but not in series III. The latter included a control device of only three pieces of polyethylene. The position of the pieces of substances in the two types of devices in series III appears in Figure 1.

Experimental procedure. All experiments were performed on non-pregnant female dogs weighing 14 to 28 kg, which were being labelled the previous day with ^{45}Ca . Cr (250 μCi b.i.d.) was given as ^{45}Ca chloride (Amersham Pharmacia Biotech) as modified by

Table 1

Distribution (per cent) of ^{51}Cr activity on vascular catheter materials exposed to arterial flow for different periods. Mean values of experiments in 7 dogs

	5 min	15 min	30 min	60 min
Polyethylene				
with lead oxide	65	42	46	40
Polyethylene	23	30	18	32
Teflon	12	28	26	28

FOSS ABRAHAMSEN (1968) The experiments were performed under light anaesthesia induced and maintained by repeated small intravenous doses of thionembal sodium (Pentothalsodium, Abbot). The animals in a fasting state were placed on a warm table and during the experiments given isotonic saline intravenously (about 2 ml/kg body weight). The following series of experiments were performed.

Series I (7 dogs) Test devices were inserted simultaneously in the aorta and the inferior vena cava; these were withdrawn after a varying period and a fresh pair inserted. Identical pairs of devices were exposed to arterial and venous blood flow in this way for 5, 15, 30 and 60 minutes.

Series II (2 dogs) Twelve test devices were inserted consecutively in the aorta of each animal. Exposures of 1, 2 and 5 minutes duration, respectively, were repeated four times.

Series III (2 dogs) Fourteen 5 minute arterial tests were performed consecutively in each animal, test and control devices being used alternately. After exposure of the devices to the bloodstream the amounts of thrombi on the pieces of material were estimated from their content of ^{51}Cr labelled platelets. The activities were measured with a 3" NaI well crystal (Autowell II Packer).

Calculations and statistical analysis The distribution of the ^{51}Cr activity as a percentage among the three materials was calculated after each test in series I and II. Comparisons were made between pairs of materials in the device in each animal by comparing the means of paired differences with Student's *t* test at the significance level of 0.05.

The thrombi formed on polyethylene in the test device in series III were used as a reference in the calculation of the amounts on the other products. For each control device the distribution of the activity on the pieces was calculated in the same way relative to that on the piece of polyethylene which was in the same position as those in the test device. Differences between the identical pieces in the control device were ascribed to sources of variation other than those due to

Table 2

Distribution (per cent) of ^{51}Cr activity on vascular catheter materials exposed to arterial flow for different periods. Mean values of four experiments in each of 2 (A and B) dogs. F. scores in brackets denote the sum of activities on the materials.

	1 min		2 min		5 min	
	A	B	A	B	A	B
Polyethylene						
with lead oxide	41	41	44	38	58	50
Polyethylene	33	34	34	39	28	32
Teflon	26	25	22	23	14	18
	100	100	100	100	100	100
	(4 009)	(3 679)	(1 782)	(3 087)	(18 671)	(9 73)

difference in materials. The former differences will be referred to as the error of the method.

A comparison of the differences between polyethylene and some other material in the test devices with those between two pieces of polyethylene placed in corresponding positions in the control devices in each animal indicated whether the differences between the compounds were larger than could be explained by the error of the method. The calculations were made with the Wilcoxon test at a significance level less than 0.05.

Results

Series I The distribution of the ^{51}Cr activity on the different materials after exposure to arterial blood flow are given in Table 1. The radioactivities were invariably largest on the polyethylene with lead oxide segment although only after 5 minutes exposure to the bloodstream were significant differences evident between all three segments. In none of the venous tests did all three pieces of materials differ from one another. The experiments in venous blood will therefore not be discussed further. The isotope activities on which these calculations were based have been reported in the previous paper on other factors (SCHLOSSMAN).

Series II The purpose of this series was to determine whether an exposure under 5 minutes would better demonstrate differences between the materials than series I. Such shorter periods are suited to demonstrate variations (Table 2). Moreover the radioactivities on the materials after 1 to 2 minutes proved to be less than 30 per cent of that after 5 minutes exposure.

Table 3

Thrombogenic properties of different vascular catheter materials Mean values of 7 experiments in each of 9
(C and D) do

	Control materials			Test materials		
	Polyethylene	Polyethylene	Polyethylene	Polyethylene	Polyethylene with lead oxide	Teflon
C	100	108	122	100	164	49
D	100	108	109	100	170	47

Series III The differences between the products were significantly larger than could be explained by the error of the method (Table 3). The result of the material test was that polyethylene with lead oxide was thus the most, and teflon the least thrombogenic of the materials examined.

Discussion

The method could demonstrate differences in thrombus formation on different materials, as judged from the amount of labelled platelets in the thrombi. That such differences could be demonstrated in arterial but not in venous blood was probably due to the fact that arterial thrombi are richer in platelets than venous thrombi. It has also previously been indicated that with the aid of the test device used the activity of the former is on the average, three to four times as large as that of venous thrombi (SCHLOSSMAN).

The exposure time most suitable for demonstrating differences between the catheter compounds obviously had a lower limit. The mechanism behind this may be explained from the findings of DUTTON *et al.* (1968). Direct microscopy of surfaces of test material in the circulation disclosed only randomly scattered platelets during the first 2 minutes but no aggregation before 3 to 4 minutes indicating a certain latency between the exposure of foreign material to the bloodstream and the adhesion and aggregation of platelets to it. Such a latency was also suggested by the observation in the present investigation that the radioactivity of the thrombi formed after exposure of the substances to arterial blood for 1 and 2 minutes was less than 30 per cent of that after 5 minutes exposure. The reason why the pertinent differences between the materials were ironed out after exposures for more than 5 minutes was probably that the lumen of the test pieces gradually became filled with thrombi. From a practical point of view, however, the shortness of the test period was a great advantage because it increased the capacity of the method.

Inter individual differences and intra individual variations make it difficult to estimate the error of the method in in vivo experiments of this type. By comparing the amount of thrombus formed in a test device with that produced in a control device in the same animal it was however possible to draw conclusions concerning differences between the compounds without calculating the error of the method.

Differences in predisposition to thrombosis between animals also precludes measurement of the thrombogenic properties of a given substance in absolute values. In other words the properties of a product can only be evaluated relative to the known properties of a reference substance used in the same animal. The examination of materials should therefore, as in series III, be performed in such a way that one or more separately tested products may be compared with a reference material whose variation includes the error of the method. The result of the test revealed that polyethylene with lead oxide was the most and teflon the least thrombogenic. The finding corroborates the opinion that teflon is a comparatively thromboresistant material (ZEITLER & SCHOOP 1970). However, as previously (NEJAD *et coll* 1968, SIEGELMAN *et coll* 1968, FORMANEK *et coll* 1970) the present investigation indicated that all such substances are thrombogenic though to a varying extent, and it is doubtful whether any synthetic product can really be non thrombogenic — a term commonly used in the literature.

The thrombogenic properties of materials has been ascribed to their physical and chemical characters (GOTT 1966). The role they play has however not yet been clarified because among other things of the difficulties in measurement. The reaction of the platelets appears to be a well founded means for this purpose and suitable also for demonstrating differences between the properties of vascular catheter substances.

Acknowledgements

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SUMMARY

The thrombogenic properties of five vascular catheter compounds, viz. teflon, polyethylene with lead oxide, polyethylene with lead oxide, polyethylene with lead oxide, and polyethylene with lead oxide, were compared in experiments in 11 dogs. The amount of labelled platelets in thrombi formed in the materials was taken as a measure of their thrombogenicity. The investigation indicated that all such materials are thrombogenic to a varying extent, and it is doubtful whether any synthetic product can really be non thrombogenic — a term commonly used in the literature.

The investigation indicated that all such materials are thrombogenic to a varying extent, and it is doubtful whether any synthetic product can really be non thrombogenic — a term commonly used in the literature.

ZUSAMMENFASSUNG

Die Thrombose hervorrufenden Eigenschaften von drei vaskulären Kathetern, erschiedener Zusammensetzung, nämlich Teflon, Polyäthylén und Polyäthylén mit Bleisöld, wurden in Experimenten an 11 Händen verglichen. Die Menge von gezeichneten Thrombozyten in gleichzeitig gebildeten Thromben auf diesen Substanzen bildeten ein Mass, deren Thrombose hervorrufenden Natur. Diesen Materialtests gingen Voruntersuchungen voraus, um eine geeignete Technik, Unterschiede nachzuweisen auszuarbeiten. Polyäthylén mit Bleisöld erwies sich als das am stärksten, und Teflon als das am wenigsten Thrombose hervorrufende Material.

RÉSUMÉ

L'auteur a comparé, au cours d'expérimentation sur 11 chiens, les propriétés thrombogéniques de trois matériaux utilisés pour faire des cathétres vasculaires: le téflon, le polyéthylène et le polyéthylène avec oxyde de plomb. Il a pris comme mesure de leur pouvoir thrombogénique la quantité de plaquettes marquées dans les thrombus formés simultanément sur ces matériaux. L'expérimentation sur ces matériaux a été précédée par des recherches pilotes destinées à mettre au point une technique permettant de mettre en évidence ces différences. Le polyéthylène avec oxyde de plomb est le matériau le plus thrombogénique et le téflon est le moins thrombogénique.

REFERENCES

- AAS, K. A. and GARDNER, F. H. Survival of blood platelets labelled with chromium-51. *J. clin. Invest.* 37 (1958) 1257.
- DUTTON, R. C., BAUER, R. E., DEDRICK, R. L. and BOWMAN, R. L. Initial thrombus formation on foreign surfaces. *Trans. Amer. Soc. artif. intern. Organs* 14 (1968) 57.
- FORMAKER, G., FRECH, R. S. and AMPLATZ, H. Arterial thrombus formation during clinical percutaneous catheterization. *Circulation* 41 (1970) 833.
- FORS, ABRAHAMSEN, A. A modification of the technique for ⁵¹Cr labelling of blood platelets giving increased circulating platelet radioactivity. *Scand. J. Haematol.* 5 (1968) 53.
- GOTT, V. L. The causes and prevention of thrombosis on prosthetic materials. *J. sur. Res.* 6 (1966) 274.
- JACOBSON, B. and SCHLOSSMAN, D. Thromboembolism of leg following percutaneous catheterization of femoral artery for angiography. Predisposing factors. *Acta radiol. Diagn.* 8 (1969) 108.
- NEJAD, M. S., KLAPER, M. A., STEGGERDA, F. R. and GIANLUCCI, C. Clotting on the outer surfaces of brachial catheters. *Radiology* 91 (1968) 248.
- SCHLOSSMAN, D. Thrombogenic properties of vascular catheter materials in vivo. A device and objective method of comparing thrombus formation on vascular catheter materials. *Acta radiol. Diagn.* 14 (1973) 97.
- SIFORDMAN, S. S., CAPLAN, L. H. and ARNES, G. P. Complications of catheter angiography. Study with oscillometry and pullout angiograms. *Radiology* 91 (1968) 251.
- ZEITLER, F. und SCHROOF, W. Der Wandel in der Indikation zur Angiographie bei der arteriellen Verschlusskrankheit. *Fortschr. Röntgenstr.* 112 (1970) 291.

USE OF ALUMINIUM TO SIMULATE ATTENUATION IN DIAGNOSTIC ROENTGEN BEAMS

ROBERT G. GOULD and JOHN HALE

In the testing and calibration of diagnostic roentgen machines it is often useful to simulate patient attenuation with aluminum filtration placed near the tube. Examples of this are the calibration of automatic exposure timers and the measurement of the exposure rate at the input phosphor of image intensifying tubes. A similar approach was used by WEYL & WARREN (1935) to investigate techniques for chest roentgenography.

While in principle water is the best phantom material it is convenient to be able to change the absorber thickness by small increments in a horizontal roentgen beam. Accordingly pressed wood was chosen to simulate patient attenuation and scatter but the water equivalent thickness of the particular batch was first determined by using the automatic brightness control system of an image intensifier as an exposure meter.

Transmission curves through the absorbers were determined by measuring with a photomultiplier tube the lumiance of a par speed intensifying screen mounted behind a thin absorbing bakelite light shield (ICRU 1962). An ionization chamber near the roentgen tube was used to monitor the constancy of the exposure rate (HALE & GLORGE 1964). The added filtration of the tube

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Table

Aluminum absorber in good geometry required to produce equal luminance of fluorescent screen as water absorber with scatter

Water thickness (cm)	Aluminum thickness (mm)							
	60 kVp		80 kVp		100 kVp		120 kVp	
	No grid	Grid	No grid	Grid	No grid	Grid	No grid	Grid
5	3.8	6.5	4.5	8.0	4.8	9.0	5.2	10.0
10	8.5	14.2	10.0	17.2	10.5	19.3	11.6	21.3
15	14.6	22.6	16.0	27.5	17.6	30.7	19.5	33.0
20	20.8	31.0	23.0	38.2	26.0	43.2	28.0	46.1
25	27.4	—	31.2	—	35.5	—	38.5	—

was 2 mm Al, and the distance between the tube target and the fluorescent screen was 2 m.

Four sets of measurements were made using the aluminum and water equivalent absorbers with and without a grid. For the aluminum data good geometry was established by using a double diaphragm system to limit the beam size to the size of the intensifying screen (11.4 cm × 14.6 cm) and placing the absorber near the tube. For the water equivalent measurements, the absorber was as close as possible to the intensifying screen enclosure. The field size was 35.6 cm × 43.2 cm. The 8:1 ratio stationary grid was placed next to the enclosure in either case. The results are shown in the Table.

Comparison of these data with the data of WEYL & WARREN (1935) show that the attenuation of the chest may be simulated by assuming that the chest has a density of 0.5 g/cm³.

Acknowledgements

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SUMMARY

A table is presented of the thickness of aluminum in good geometry required to produce equal luminance of par speed intensifying screens as a water absorber in contact with the cassette. Results are presented for the potential range from 60 kVp to 120 kVp with and without an 8:1 grid.

ZUSAMMENFASSUNG

Es wird eine Tabelle über die Dicke von Aluminium gegeben die in geeigneter Form gebraucht wird um gleiche Luminanzwerte von par speed Verstärkerfolien als ein Wasserabsorber in Kontakt mit der Kassette hervorzubringen. Ergebnisse für den Spannungsbereich zwischen 60 kVp und 120 kVp mit und ohne ein 8:1 Schichtverhältnis des Streustrahlrasters werden angelegt.

RÉSUMÉ

Les auteurs présentent un tableau de l'épaisseur d'aluminium de forme convenable nécessaire pour donner à des écrans renforceurs de rapidité moyenne une luminance égale à celle d'un absorbeur en eau au contact de la cassette. Les résultats sont présentés pour des tensions allant de 60 kVp à 120 kVp, et ce et sans une grille de rapport 8.

REFERENCES

- HALE, J. and GROWER, D. L. Physical factors in cinefluorography: exposure meter and phantom materials. *Amer. J. Roentgenol.* 97 (1964) 1118.
- ICRU Report 10: Methods of evaluating radiological equipment and material. ICRU, Washington, 1962.
- WERT, C. and WARREN, JR. S. R. Apparatus and techniques for roentgenography of the chest. p. 170. Charles C. Thomas, Springfield, Illinois, 1953.

RELATIONS BETWEEN BLOOD FLOW ARTFRIAL CROSS SECTIONAL AREA AND TOTAL AND CORTICAL VOLUMES OF THE KIDNEY

J GOTHILIN V HEGEDUS and T OLIN

The information obtainable by angiography of the kidney is mainly morphologic although one of the more important parameters in renal disorders is the blood flow. The present investigation was undertaken to establish whether any important correlations exist between the various morphologic dimensions obtained by nephroangiography and the renal blood flow and related constants determined by a dye dilution technique.

Material and Methods Angiography and the renal blood flow determination were performed in 38 kidneys 14 of whom were normal. The angiograms were obtained in two projections to provide a three dimensional conception of the kidney (HEGEDUS 1972). The total volume and the superficial continuous cortical volume (HEGEDUS & FAARUP 1972) as well as the cross sectional area of the renal artery were measured. The blood flow was determined by the dye dilution technique described by GOTHILIN & OLIN (1970 1973). The material is presented in Tables 1 and 2. The 14 normal kidneys were from patients referred for probable primary carcinoma, pain in the back or earlier bacteriuria.

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Table 1
Different parameters in normal kidneys

Ca	Age	Sex	Side	RAC	TV	CV	CORT	RBF	VV	VR	MTT
1	16	M	R	38	138	79	57	319	42	28	7.9
			L	50	157	84	52	312	47	29	9.0
2	40	F	R	44	116	70	60	455	69	25	9
3	33	F	L	33	86	47	54	319	47	30	8.9
4	12	M	R	44	124	66	54	556	66	18	1
			L	44	104	61	58	492	69	21	8.4
5	53	F	L	44	156	83	52	300	46	30	9
6	31	F	R	53	93	44	58	458	53	17	7.5
7	52	F	R	58	113	10	53	444	67	20	9.1
8	49	M	R	50	140	73	52	487	86	18	10.6
			L	57	172	86	50	461	70	19	9.1
9	15	M	R	28	9	48	51	490	61	22	7.5
10	31	F	R	28	88	4	51	278	46	21	9.9
			L	28	109	60	53	305	50	19	9.9
Range											
	1-53			28-57	86-172	45-86	50-60	278-556	42-86	17-30	7.1-10.6
				14	14	14	14	14	14	14	14
				59.9	120.8	63.4	54.1	404	58.6	22.6	8.8
SD				9.2	27.8	14.2	3.1	93.3	12.9	4.8	1.0
SE				2.4	7.4	3.8	0.8	24.9	3.3	1.3	0.3
t				16.3	16.2	17.3	63.3	16.2	17.0	17.7	37.4

RAC Cross sectional area of the renal artery (mm²) calculated according to the formula

$$RAC = \pi \frac{(\text{diameter of the renal artery})^2}{4}$$

TV Total volume of the kidney (ml)

CV Volume of the superficial corticomedullary cortex of the kidney in (ml)

CORT Superficial corticomedullary cortex volume as percentage of total volume of kidney

RBF Renal blood flow (ml/min) measured by the dilution technique

MTT Mean transit time (seconds)

VV Vascular volume (ml) calculated as the product of the mean transit time in seconds and the RBF (ml/second)

VR Vascular resistance a peripheral resistance unit is calculated as the mean arterial pressure in mm Hg divided by the RBF (ml/second)

Table 2
Different parameters in diseased kidneys

Case	Age	Sex	Sid	RAC	TV	CV	CORT
11	1	M	R	50	264	148	56
12	19	F	R	50	168	91	54
			L	44	187	104	55
13	21	F	L	64	181	101	56
14	38	M	R	38	143	73	51
			L	50	146	72	49
15	76	M	L	64	186	89	49
16	54	F	L	24	153	74	48
17	55	M	R	44	196	85	44
18	33	F	R	38	149	71	47
19	27	F	R	44	121	68	56
20	16	M	R	28	8	47	56
21	58	F	R	20	90	40	45
			L	20	109	40	40
22	53	F	R	24	75	43	57
			L	24	107	58	54
23	60	F	L	38	165	76	46
24	63	F	L	38	10	56	53
25	62	F	R	20	72	46	62
			L	20	108	49	45
27	34	F	R	38	172	74	4
28	19	M	R	50	119	69	51
29	63	M	L	28	97	45	46
36	72	F	L	24	124	70	56
Range 10-79				20-64	72-264	40-148	40-61
				24	24	24	24
x				36.8	138.1	70.1	50.8
SD				13.6	46.3	23.0	5.6
SE				2.8	9.4	5.1	1.1
t				13.2	14.6	13.7	44.3

No cases of renal haematuria were included: those with large deformities of the kidneys were also excluded. The diagnosis varied widely in the diseased kidneys (Table 2).

Results

Good correlation existed between the various morphologic data obtained from the angiograms in normal as well as in diseased kidneys. Fig. 1 indicates that the

Table 2 (cont.)

RBF	VV	MTT	Diagnosis	
680	127	15	11.4	Acute glomerulonephritis
379	58	28	9.1	
640	106	17	9.9	
578	73	24	5	
498	68	20	8.9	Nonacute glomerulonephritis
394	62	26	9.4	
311	54	30	8.5	
583	79	20	8.1	
508	79	29	9.3	Compensatory hyperplasia
5	80	17	7.3	Ren mobilis
337	51		7.1	Pyelonephritis
317	41	39	7.7	
480	51	15	6.3	
412	40	18	6.5	
399	51	30	9.5	Cyst
336	59	28	9.2	
59	57	28	8.7	
204	37	35	8.8	
206	41	55	13.9	Nephrosclerosis
208	48	57	15.7	Nephrosclerosis + cyst
509	58	27	11	Hydronephrosis
377	53	39	11.6	Scleroderma
231	50	28	7.5	Hypertensive disease
230	46	26	12.1	Fanconi syndrome
206-680	37-127	15-57	6.3-15.7	
24	24	24	24	
390.5	61.5	27.3	9.3	
139.7	21.2	10.5	2.5	
28.3	4.3	2.1	0.5	
13.9	14.2	12.8	19.8	

total volume and the cortical volume are correlated to the cross sectional area of the renal artery in both groups. This means that a small artery is associated with a small kidney and a small cortical volume. The functional parameters blood flow and vascular resistance do not usually exhibit a strong correlation to the morphologic data (Fig. 2); the cross sectional area of the renal artery reflects the blood flow only to a minor extent ($r=0.3$, $t=1.2$ in normal kidneys; $r=0.4$, $t=1.8$ in diseased kidneys). In diseased kidneys, however, good correlation existed between α flow and the cortical as well as the total

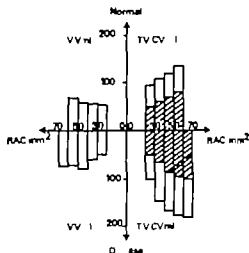


Fig. 1. The relations between the cross sectional area of the renal artery (RAC) and the total volume (TV), cortical volume (CV, filled staples) and vascular volume (VV) of the kidney. Normal kidney above diseased kidney below.

volumes of the kidney. The vascular volume calculated from the dye dilution curve, was also correlated to the total and cortical volumes in diseased kidneys, although not in normal ones (Table 3). The vascular volume displayed some correlation to the cross sectional area of the renal artery ($r=0.4$ to 0.5 , $t=2.0$ to 2.1) in both normal and diseased kidneys. No significant correlation in normal kidneys between the vascular resistance and the total and cortical volume was evident although some was observed in diseased kidneys ($r=-0.4$ to -0.5 , $t=2.1$ to 2.5).

Discussion

A comparison between the renal blood flow and related parameters measured directly and the total and continuous cortical volumes of the kidney appears hitherto not to have been performed. The technical aspects of the dye dilution technique have been described in detail by GOTHILIN & OLIN (1973); the method of determining the total volume and continuous cortical volume of the kidney from nephroangiograms has been described by HEGEDUS & FÄRUP (1972).

A significant correlation between a two-dimensional estimation of renal size and the cross sectional area of the renal artery was demonstrated by LUDV (1965) and LUDV (1967) in cases of pyelonephritis. The present authors have made a three dimensional analysis of the cortical and total volumes and recorded good correlation in both instances (Table 3, Fig. 1).

LUDV *et al.* (1967) in another investigation determined the effective renal plasma flow by a clearance technique and demonstrated good correlation between the flow and the cross sectional area of the renal artery in some groups of diseased

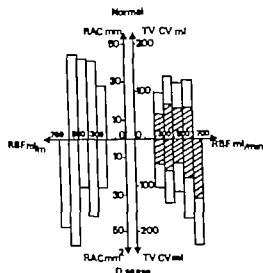


Fig. 2 Right: The relations between renal blood flow (RBF) and the total volume (TV) and cortical volume (CV, filled staples) of the kidney. Left: The relation between renal blood flow (RBF) and the cross sectional area of the renal artery (RAC). Normal kidney above diseased kidneys below.

kidneys with decreased blood flow. The present authors measured the total renal blood flow with a dye dilution technique and related it to three-dimensionally determined total and cortical volumes and in agreement with LUDIN and LUDIN *et coll.* observed good correlation only in diseased kidneys; contrary to LUDIN *et coll.* however only slight correlation was recorded between the blood flow and the cross sectional area of the renal artery in these kidneys. The only explanation to be offered for this discrepancy would appear to be that the material contains too few kidneys with advanced lesions.

In the estimation of cortical volume a degree of inaccuracy remains since the method does not include quantitative assessment of the volume of the columns of Bertin. The amount of tissue in these structures is 13 to 34 per cent of the total cortical volume (HJØRNBUS & FAARUP). Most patients in the group with a renal blood flow of 400 to 500 ml (Fig. 2) had large columns of Bertin which explains the relatively low value for continuous cortical volume. The cortical blood flow is about 90 per cent of the total renal blood flow (BARON 1963) and therefore good correlation between the renal blood flow and the cortical volume ought to be expected. This was not evident in the normal kidneys although well defined in the group of diseased kidneys (Table 3). The cortex is composed not only of glomeruli but of several other structures as well. The flow resistance in the nephrons depends *inter alia* on the tone of the afferent arteriole and on the amount and the calibre of the capillaries in the glomerular tuft. The absence of correlation between the renal blood flow and the cortical volume in normal kidneys may possibly depend upon the large reserve capacity of the renal parenchyma.

Table 3

Relations between various parameters within the groups of normal and diseased kidneys

	Normal			Diseased		
		t	p		t	p
RAC-TV	0.8	5.2	< 0.01	0.7	4.6	< 0.01
RAC-CA	0.8	5.1	< 0.01	0.7	4.7	< 0.01
RAC-VV	0.5	2.0	< 0.05	0.4	2.1	< 0.05
RAC-RBF	0.5	1.2	< 0.1	0.4	1.8	< 0.05
TV-VV	0.0	0.0		0.7	4.2	< 0.01
TV-RBF	0.0	0.1		0.7	4.2	< 0.01
CA-VV	0.1	0.4		0.8	7.0	< 0.01
CA-RBF	0.0	0.1		0.7	4.2	0.01
TV-V R	0.2	0.7		-0.5	2.5	0.01
CA-V R	0.3	1.0		-0.4	2.1	0.05

A certain correlation exists between the cross sectional area of the renal artery on the one hand and the total volume, cortical volume, vascular volume and renal blood flow on the other (Table 3). It is not known precisely how the renal artery senses the flow and then adjusts its calibre to it. A possible explanation may be that the stress of the arterial wall triggers a reaction that keeps this stress relatively constant. The circumferential stress (σ) of the arterial wall is double the longitudinal stress and is directly proportional to the pressure (P) and the inner diameter of the vessel (v) and inversely proportional to the thickness of the wall (s):

$$\sigma = \frac{P \cdot d}{s}$$

If the vascular resistance in the kidney be increased the pressure in the renal artery will also rise. The response will be a diminution in the calibre of the artery increasing the thickness of the arterial wall. With diminished vascular resistance in the kidney the pressure in the artery will be reduced and an inverse reaction will result in widening of the renal artery and reduction in the thickness of the arterial wall. The stress in the arterial wall will thereby be kept almost constant (THIRAU & KRANER 1959).

Some general conclusions may be drawn from the results of the present investigation. If at urography the kidney be small the cross sectional area of the renal artery is likely also to be small and the renal blood flow low. Estimation of the renal blood flow from the cross sectional area of the renal artery as defined by

nephroangiography is inadvisable as the correlation between these parameters is very low. Nephroangiography in one plane may make it possible to estimate the volume to some extent but three dimensional analysis is much more accurate. This will permit assessment of the renal blood flow in diseased kidneys in which the total and cortical volumes are correlated to the renal blood flow. Conversely if the blood flow be determined by clearance or by gamma camera scintigraphy and proves to be below normal this may indicate that the kidney and its cortex are undersized.

Acknowledgements

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SUMMARY

The renal blood flow and related parameters determined by a dye dilution technique were compared with the cross sectional area of the renal artery and the total and cortical volumes of the kidney established by angiography. The correlation between the renal blood flow and the morphological data was good only in diseased kidneys in which the cortical and vascular volumes were also well related. The correlation between the cross sectional area of the renal artery and the total and cortical volumes was determined in both normal and diseased kidney.

ZUSAMMENFASSUNG

Die Nierendurchblutung und zugehörige Parameter die mit einer Farbstoffverdünnungsmethode bestimmt worden waren wurden mit dem Querschnitt der Nierenarterie, dem Gesamtvolumen und dem kortikalen Volumen der Niere die durch Angiographie festgestellt worden waren verglichen. Die Korrelation zwischen der Nierendurchblutung und den morphologischen Daten war nur bei kranken Nieren gut bei denen auch die kortikalen und vaskulären Volumina gut einander zugeordnet waren. Die Korrelation zwischen dem Querschnitt der Nierenarterie und dem Totalvolumen und dem kortikalen Volumen wurden an sowohl normalen als auch kranken Nieren bestimmt.

RÉSUMÉ

Le débit sanguin renal et les paramètres qui y sont rattachés déterminés par une technique de dilution d'un colorant ont été comparés avec la surface de la section de l'artère rénale et avec le volume total du rein et le volume cortical du rein établis par angiographie. La corrélation entre le débit sanguin renal et les données morphologiques n'est bonne que sur les reins malades pour lesquels le volume cortical et le volume vasculaire sont aussi en bonne corrélation. La corrélation entre la surface de l'artère rénale et le volume total et le volume cortical est déterminée sur des reins normaux et sur des reins pathologiques.

REFERENCES

- BARCEY A. Cortical and medullary blood flow in the kidney. In: Progress in nephrology, p. 398. Edited by E. Kass. P. A. Davis Co. Philadelphia 1965.
- GÖTHLIN J. och OLIN T. Nefroangiografi kompletterad med blodflödesmätning enligt färgspädningsmetoden. (In Swedish.) Nord. Med. 84 (1970) 1317.
- — Dilution technique with nephroangiography for the determination of renal blood flow and related parameters. Acta radiol. Diagnosis 14 (1973) 113.
- HEGEDUS A. Three-dimensional estimation of renal shape and volume: angiography. Acta radiol. Diagnosis 11 (1972) 87.
- and FAARUP P. Cortical volume of the normal human kidney. Correlated angiographic and morphologic investigations. Acta radiol. Diagnosis 12 (1972) 481.
- LUDWIG H. Tomographische Bestimmung der Nierengröße. Fortschr. Röntgenstr. 95 (1961) 215.
- Zur quantitativen Bestimmung des relativen Nierenarterienkalibers. Fortschr. Röntgenstr. 103 (1965) 609.
- Radiologic estimation of kidney weight. Acta radiol. Diagnosis 6 (1967) 561.
- ELIAS M., FEHR H. and THORLEIF H. Correlation of renal size, renal artery caliber and effective renal plasma flow in man. Acta radiol. Diagnosis 6 (1967) 296.
- MOELL H. Size of normal kidneys. Acta radiol. 46 (1956) 640.
- Kidney size and its deviation from normal in acute renal failure. A roentgenographic study. Acta radiol. (1961) Suppl. No. 206.
- TITMANN K. und KRAMER K. Die Reaktionsweise der glatten Muskulatur der Nierengefäße auf Dehnungsreize und ihre Bedeutung für die Autoregulation des Nierenkreislaufes. Pfügers Arch. ges. Physiol. 268 (1959) 188.

RENAL BLOOD FLOW IN MOBILE KIDNEYS MEASURED BY A DYE DILUTION TECHNIQUE IN COMBINATION WITH ANGIOGRAPHY

J GÖTHLIN

A mobile kidney often appears to constitute the only possible explanation of renal pain. A small material offered a suitable opportunity for examining this assumption by urography and nephroangiography in conjunction with the determination of renal blood flow. It was subsequently considered that publication of the results might prove of some general interest.

Material and Methods Six women were referred for nephroangiography with the diagnosis of mobile kidney. Four of the patients had pain in the right loin, in 3 of these on movement. Three of the 4 had had episodes of proteinuria and bacteriuria. Of the remaining two patients one had constant proteinuria and the other episodes of bacteriuria without pain. Urography revealed a mobile kidney on the right side in all patients. Slight widening of the pelvis and the ureter with some kinking of the latter was evident in 2 of the patients. Arteriography and phlebography were performed in the supine and erect positions. The renal blood flow was measured by a dye dilution method in conjunction with angiography as

Table

Renal blood flow and mean transit time in the supine and erect positions

Case	Age	Sex	RAD _s	RAD _e	S	RBF	RBF	MTT	MTT
1	33	F	4.9	3.4	R	352	633	7.5	7.8
2	29	F	4.5	3.1	R	509	422	9.9	9.9
3	43	F	3.8	3.2	R	358	323	10.9	10.9
4	27	F	5.3	3.8	R	337	335	7.1	6.4
5	22	F	4.9	3.9	R	306	338	9.6	9.5
6	32	F	4.5	—	R	(278)	—	(9.9)	—
			(4.5)	—	L	(303)	—	(9.9)	—
Mean	31		4.5	3.5		453	456	9.0	8.9
Range	22—43		3.8—	3.1—		337—	323—	7.1—	6.4—
			5.3	3.9		552	633	10.9	10.9

RAD_s Diameter of renal artery in supine positionRAD_e Diameter of renal artery in erect position

S Localization of kidney R right L left

RBF Renal blood flow in supine position

RBF Renal blood flow in erect position

MTT Mean transit time in supine position

MTT Mean transit time in erect position

described by OLIN & GÖTHLIN (1971) and GÖTHLIN & OLIN (1970, 1973) also with the patients supine and erect without support. One of the patients had bilateral blood flow determinations made while only the right kidney was examined in the others. All the blood pressures were normal.

Two patients with dilatation of the pelvis later underwent nephropexy.

Results

The mobile kidneys rotated with the hilum upwards during the procedures with the patient erect and became displaced downward for 3.8 to 4.5 cm with stretching of the main artery and vein; no changes in the smaller vessel were evident and the parenchymatous phase of the cortex was unaltered. In the erect position kinking of the ureter was demonstrated in 2 patients and pain was experienced during examination in one patient. The diameter of the renal artery decreased by a mean of 1.0 mm in the erect position and the diameter of the renal vein by a mean of 1.2 mm. The renal blood flow and mean transit time in the supine and erect positions appear in the Table; minor changes occurred when the position was altered but there was no constant trend.

DISCUSSION

Mobile kidneys are common, especially on the right side and in women (HIND 1931 CAMPBELL 1967). Most patients have no symptoms but a few experience some pain in the loin according to THOMSON WALKER (1948) torsion of the renal vessels may sometimes cause pain. No change of blood flow was revealed in the erect position nor did the mean transit time change in the present investigation. Some stretching and narrowing of the main vessels to the kidney but no kinking was evident at angiography. The total vascular resistance of the kidney may hardly be changed by such alterations. Similar angiographic appearances have been described by EIE & SANDER (1971). The reason for pain in mobile kidneys is not clear. It may sometimes be due to ureteric kinking with urinary stasis, but in others this type of mechanism may be eliminated. Another possible explanation may be stretching of the nerves to the kidney that surround the renal artery in a rich network. These are largely vasomotor but sensory fibres also pass to the pelvis calyces and capsule and react to distension (KRAUSE 1969). Two patients of the material were subjected to nephropexy. The urography had been normal but the pain persisted. Nephropexy seems to be indicated mainly for treating ureteric kinking with subsequent dilatation but the effect of operation on pain is unreliable. The present investigation produced no suggestion that the pain might be due to renal ischemia.

Acknowledgements

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SUMMARY

Six patients with a right mobil kidney were examined by urography and nephro-angiography with determination of the renal blood flow. Some slight stretching and narrowing of the main vessels to the kidney occurred in the erect position during the procedures but the blood flow was unaffected. There was thus no evidence that the pain experienced by one patient was due to renal ischaemia.

ZUSAMMENFASSUNG

Sechs Patienten mit einer rechtsseitigen bei geleglichen Niere wurden durch Urographie und Nephroangiographie mit Bestimmung der Nierendurchblutung untersucht. Eine leichte Dehnung und Verengung der Hauptgefäße der Niere erfolgte in aufrechter Lage bei diesen Verfahren wobei jedoch die Durchblutung unbeeinträchtigt war. Es liegt somit kein Zeichen dafür vor dass die bei einem Patienten hervorgerufenen Schmerzen auf einer Ischämie der Niere beruhen.

RÉSUMÉ

Six malades ayant un rein droit mobile ont été examinés par urographie et par néphroangiographie avec mesure débit sanguin renal. Au cours de ces examens en position debout les principaux ansesaux allant au rein ont été un peu étirés et rétrécis, mais le débit sanguin est resté inchangé. Il n'y a eu donc pas de preuve que la douleur qu'éprouvait un de ces malades était due à une ischémie renale.

REFERENCES

- CAMPBELL M. Anomalies of the kidney. In: Urology. Second edition. Vol. II. p. 1588. Saunders Co. Philadelphia and London 1967.
- ERL H. and SANDER S. Angiographic findings in the mobile kidney. Scand. J. Urol. Nephrol. 5 (1971) 48.
- GOTTLIN J. och OLIN T. Nefroangiografi kompletterad med blodflödesmätning enligt färgspänningsmetoden. (In Swedish.) Nord. Med. 84 (1970) 1317.
- — Dye dilution technique with nephroangiography for the determination of renal blood flow and related parameters. Acta radiol. Diagnosis 14 (1973) 113.
- KIDD F. Acquired renal dystopia or movable kidney. J. Urol. 26 (1931) 327.
- KRAUSE W. Nerven der Niere. I. Encyclopedia of urology. Band VIII. p. 110. Springer Verlag. Berlin Heidelberg New York 1969.
- OLIN T. and GOTTLIN J. Determination of renal blood flow in humans in connection with renal angiography. I. Radiology. p. 182. Excerpta Medica Foundation. Amsterdam 1971.
- THOMSON WALKER J. Genito urinary surgery. Cassell & Co. Ltd. London Toronto Melbourne Sydney Wellington 1948.

RELATIONSHIP BETWEEN RENAL SIZE AND FUNCTION IN NORMAL SUBJECTS

M. J. F. ANDERSEN and C. E. MOGENSEN

Renal function varies to some degree in normal subjects. A recent investigation in 31 normal young male patients revealed a mean glomerular filtration rate (GFR) of $111 \text{ ml/min} \pm 13$ (SD) with a range of from 88 to 145 ml/min ; the mean renal plasma flow (RPF) was $568 \text{ ml/min} \pm 93$ (SD) with a range from 372 to 839 (MOGENSEN 1971 b). These values are of the same order of magnitude as those presented by other workers (WESSON 1969). Renal size is also known to vary within certain limits in normal man (MOELL 1961).

The purpose of the present investigation was to determine whether a correlation between the roentgenologic size of the kidney and renal function as measured by GFR and RPF could be demonstrated. Such a relationship has earlier been evident in patients with hypertension or various renal disorders (LADROGOD & PEDERSEN 1968). The conditions in normal human subjects appear so far not to have been examined although this would seem to be essential if the evaluation in disease of the kidney is to be of value.

Material and Methods Twelve normal young male subjects (medical students) aged 23 to 30 (mean 25.5) years, none with a history or signs of renal disease, were examined. Their height ranged from 168 to 192 (mean 178.6) cm and

Table

Renal function and size measurements

Sub ject	Body sur face m	GFR	RPF	Filtration fraction GFR/ RPF	Roentgenographic renal size				Area (right + left) cm	Area cor rected to 1.73 m
					Right kidney		Left kidney			
					Length cm	Width cm	Length cm	Width cm		
1	1.6	132	769	0.17	14.5	6.2	15.2	7.2	199	909
	1.85	123	638	0.19	13.7	7.0	15.2	6.6	183	171
3	1.96	94	412	0.23	12.0	5.8	12.2	5.9	14	1.3
4	1.91	118	622	0.19	13.7	8.0	15.0	8.0	230	208
	1.78	113	609	0.19	14.5	6.0	13.9	6.8	181	176
6	1.94	112	50	0.20	14.0	6.8	13.3	7.0	178	168
7	1.74	123	480	0.26	13.0	6.0	13.8	6.5	168	167
8	1.87	105	453	0.23	12.5	6.3	13.0	6.0	157	145
9	1.85	141	697	0.20	13.3	7.0	12.4	7.3	184	179
10	1.9	120	517	0.23	14.7	6.5	13	6.8	187	166
11	2.11	124	491	0.25	1.6	7.5	14.0	7.6	208	171
12	1.99	96	356	0.27	13.2	6.0	14.2	6.3	169	147
Mean	1.883	116.8	550.8	0.218	13.56	6.59	13.63	6.83	183.0	168.8
±SD	0.122	13.77	121.30	0.032	0.818	0.682	0.911	0.629	23.19	23.74

body weight from 55 to 83 (mean 70.9) kg. The data on body surface are based on the nomograms of DUBOIS & DUBOIS (1916).

Renal function tests The GFR and RPF were measured by the classical constant infusion technique with Iothalamate (Amersham) as filtration marker. The clearance of ¹²⁵I hippuran (Amersham) was used for estimating the RPF. The technique has been described in detail elsewhere (MOGENSEN 1971 b). The subjects were examined fasting in the morning, three or four periods being used in each test. All values were corrected to 1.73 m² body surface. It has previously been demonstrated that labelled Iothalamate is a reliable filtration marker (ELWOOD et al. 1967; SKOV 1970; MOGENSEN 1971 b). Furthermore, the clearance of labelled hippuran provides a reliable estimation of the RPF (MAGNUSSEN 1962; SUMMERS et al. 1967; MOGENSEN 1971 b).

Renal size measurements The size of the kidney was measured in roentgrams at a FFD of 110 cm obtained with ureteric compression following the injection of 20 to 40 ml Conray R (400 mg iodine/ml) as contrast medium.

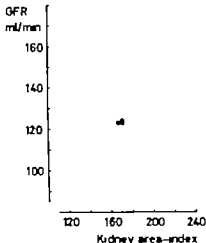


Fig. 1 The glomerular filtration rate plotted against the renal area index in 12 normal subjects

The length and width of the kidneys were measured 10 minutes after the injection if the kidneys were then well delineated only occasionally were the measurements made at a later time or in a tomogram. The following measurements were performed (see MOELL 1961)

Length greatest distance from pole to pole in cm

Width greatest distance from lateral renal surface to tangential line of medial borders of the kidney in cm

Renal area product of length and width in cm = kidney area index

Renal weight calculated on the basis of data presented by MOELL (1961)

The kidney size measurements were performed by one of us (M. J. F. A.) who was unaware of the results of renal function tests

Results

Renal function The results appear in the Table. The mean GFR was 116 ± 13.77 (SD) ml/min with a range from 94 to 141 ml/min. The corresponding values for the RPF were 550.8 ± 121.30 (SD) ranging from 377 to 769 ml/min. The mean percentage coefficient of variance for the three clearance periods in each test was 3.8 and 4.1 respectively. These values are somewhat lower than those obtained in a material presented elsewhere (MOELL 1971 a, b).

Renal size The roentgenographic data are also included in the Table. The mean lengths of the right and left kidneys were 13.56 ± 0.91 (SD) cm and 13.63 ± 0.91 (SD) cm respectively with the mean width 6.5 ± 0.7 (SD) cm.

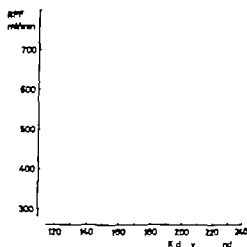


Fig. 2 The renal plasma flow plotted against the renal area index in 12 normal subjects

(SD) and 6.83 ± 0.629 (SD) respectively. The mean area index of both kidneys (product of length times width) was $183.0 \text{ cm} \pm 23.19$ (SD) and corrected to 1.73 m^2 body surface becoming $168.8 \text{ cm} \pm 23.74$ (SD). The mean calculated renal weight was $321.3 \text{ g} \pm 54.6$ (SD) also corrected to 1.73 m^2 .

Correlations. It appears from figures 1 and 2 that clear correlation exists between both the GFR and RPF and roentgenographic renal size, the coefficients of correlation being 0.68 and 0.80 respectively ($p < 0.01$ and $p < 0.001$ respectively). No correlation was evident in the present material between the actual kidney size and weight and height or body weight of the subjects.

The results obtained indicate that the GFR and RPF may be expressed per gram calculated kidney weight as $0.37 \text{ ml/g/min} \pm 0.041$ (SD) and $1.57 \text{ ml/g/min} \pm 0.171$ respectively.

The percentage coefficient of variance for RPF is 22.0. However, when the flow is expressed as per gram calculated kidney weight, the value is reduced to 13.4 per cent. These values for the GFR are 11.8 per cent and 11.1 per cent respectively, so that no reduction in the coefficient of variance can be demonstrated.

Discussion

A clear positive correlation between renal function as judged by the RPF and GFR and renal size was demonstrated in the present investigation. This has earlier been reported in patients with hypertension and other disorders affecting the kidney (LADROGOD & PEDERSEN) but so far not in normal subjects. A correlation between size and function has also been demonstrated in the normal dog (OLESEN & GENSTER 1970).

It is likely that the size of a normal organ determines the level of function. The GFR and RPF should therefore be presented as the dependent variables as in figures 1 and 2. The blood flow should however also be considered as a factor that may determine the size of the kidney. Pentothal anaesthesia with a resultant fall in blood pressure has been known to produce a decrease in renal size (Hobson 1961) the plasma flow was not measured but it is likely that the drop in blood pressure was associated with a decrease in the blood and plasma flow to the kidney. Variation in the size of renal arteries may influence the renal plasma flow and subsequently the size of the kidney in normal subjects. The authors have however no data to test this hypothesis.

Urography was employed in the present investigation of the size of the kidney. Moëll used conventional roentgenograms for the purpose. The passage of contrast medium through the kidney may produce some swelling and result in increased size. The present normal values are also slightly higher than those given by Moëll. The weight of the kidney may therefore be slightly overestimated when calculated from the diagram presented by Moëll. Such a small overestimation is, however, probably without significance for comparative purposes.

It is worth mentioning that the considerable variation in the RPF, the coefficient of variance being 22.0 per cent even after correction for body surface, is markedly reduced when the flow is expressed as ml/g renal weight, namely to 13.4 per cent. The coefficient of variance for the GFR is at the 11 to 12 per cent level both before and after correction for organ size. These findings suggest that the GFR, irrespective of kidney size, is more closely regulated.

Several factors are known to influence renal function in the normal state, namely age, sex, as well as the protein content of the diet (Wesson 1969). It is also accepted that the kidney is generally smaller in females and the elderly. Other factors affecting renal function may also influence the size of the kidney.

An investigation of the relationship between renal size and function in various pathologic states would doubtless prove of interest. It is well established that the GFR is markedly increased in young short term diabetics (Stalder et coll 1960, Ditzel & Schwartz 1967, Mogensen 1971 a, b). Work is now in progress to evaluate renal size in such patients so as to determine whether this is associated with increased function.

Acknowledgement

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SUMMARY

Determinations of renal function and size were performed in 12 young normal male subjects. Positive correlation between both glomerular filtration rate and renal plasma flow and kidney size as measured from roentgenograms was demonstrated.

ZUSAMMENFASSUNG

Bestimmungen der Nierenfunktion und Nierengröße wurden an 12 jungen normalen männlichen Personen vorgenommen. Eine positive Korrelation zwischen sowohl der Glomerulus Filtration als auch der Nieren Plasma Durchstromung und der roentgenologisch gemessenen Nierengröße wurde nachgewiesen.

RÉSUMÉ

Les auteurs ont étudié la fonction rénale et les dimensions des reins chez 12 sujets masculins normaux. Ils ont mis en évidence une corrélation positive entre le test de filtration glomérulaire et le débit plasmatique rénal d'une part et les dimensions des reins mesurées sur les radiographies d'autre part.

REFERENCES

- DRITZEL J. and SCHWARTZ M. Abnormally increased glomerular filtration rate in short term insulin-treated diabetic subjects. *Diabetes* 16 (1967) 264.
- DUBOIS D. and DUBOIS E. A formula to estimate the approximate surface area if height and weight be known. *Arch intern Med* 17 (1916) 863.
- ELWOOD C. M., SIGMAN E. M. and TROGER C. The measurement of glomerular filtration rate with 125 I sodium iothalamate. (Conroy) *Brit J Radiol* 40 (1967) 581.
- HODSON C. J. Physiological changes in size of the human kidney. *Clin Radiol* 12 (1961) 91.
- LADENBERG J. and PEDERSEN F. Relationship between roentgenological size of the kidney and the kidney function. *J Urol* 99 (1968) 239.
- MAJUMDAR G. Kidney function studies with 131 I tagged sodium orthoiodohippurate. *Acta med scand* 171 (1962) Suppl No 378.
- MOELL H. Kidney size and its deviation from normal in acute renal failure. *Acta radiol* (1961) Suppl No 206.
- MOGENSEN C. E. (a) Kidney function and glomerular permeability to macromolecules in early diabetes. *Scand J clin Lab Invest* 28 (1971) 79.
- (b) Glomerular filtration rate and renal plasma flow—short term and long term juvenile diabetes mellitus. *Scand J Clin Lab Invest* 28 (1971) 91.
- OLESEN S. and GUTTER H. G. Estimation of renal volume and function in dogs from the radiological appearance. *Invest Urol* 7 (1970) 363.
- SARON P. E. Glomerular filtration rate in patients with severe and very severe renal insufficiency. *Acta med scand* 187 (1970) 419.
- STALDE G., SCHMID R. and WOLFF M. A. Funktionelle Mikroangiopathie der Nieren beim behandelten Diabetes Mellitus im Kindesalter. *Dtsch med Wochr* 85 (1960) 346.
- SUMMERS R. F., COVEY J. P., WELLS C. and COLLE C. Determination of simultaneous effective renal plasma flow and glomerular filtration rate with 131 I-orthoiodohippurate and 125-iodiothulin. *J Lab clin Med* 69 (1967) 919.
- WATSON L. C. *Physiology of the human kidney*. Grune & Stratton New York 1967.

ANGIOGRAPHIC DIAGNOSIS OF INFLAMMATORY DISEASE OF THE PANCREAS

ULF TYLÉN and BO ARNESENJO

Angiography has in recent years become an important method in the evaluation of pancreatic disease. Most reports of the findings have so far dealt with the diagnosis of carcinoma in which a high degree of accuracy is now achieved (LUTENBERG 1965, BOOKSTEIN et coll 1969, LUCHNER et coll 1970, ROJSEW 1970, OLSSON 1970, BUCHHEIMER et coll 1971). Differentiation between carcinoma and pancreatitis is however often difficult and a thorough knowledge of the vascular changes in the latter is therefore necessary to increase further the accuracy of angiographic investigations (BAUM et coll 1965, RANNINGER & SALDINO 1966, NEUBER & POLLARD 1967, SAMMONS et coll 1967 and MOSKOWITZ et coll 1968).

A more dynamic attitude towards surgical treatment in inflammatory disease of the pancreas has gradually gained acceptance and operations directly on the pancreas in this condition are now more frequently performed than in the past (WARREN et coll 1964, CREUTZFELDT et coll 1970, DIXON & ENOLERT 1971). Operation may bring relief from pain, and the risk of complications such as acute hemorrhagic necrosis, abscess formation, diabetes mellitus or severe gastro-intestinal bleeding may be reduced. Angiography may offer valuable information

in the preoperative evaluation of the patient further emphasizing the importance of familiarity with the angiographic appearances in inflammatory disease of the pancreas.

Attention must be drawn in the discussion of angiographic changes in pancreatitis to the often neglected fact that the clinical diagnosis is difficult and that two main types of pancreatitis exist: the chronic and the acute, both occurring in relapsing form. The chronic type leads to progressive sclerosis and destruction of the pancreatic parenchyma with persistent reduction in exocrine function; ultimately the endocrine function may also be impaired. This process may cause abdominal pain, steatorrhea and diabetes mellitus (COMFORT et coll 1946 FITZGERALD et coll 1963 CREUTZFELDT et coll 1970 LEVAT et coll 1970). Excessive alcoholic consumption is considered a significant contributing factor to the development of the condition and in these patients pancreatic calcifications are common. Some authors regard calcifying chronic pancreatitis as separate and different from the non calcifying type (SARLES et coll 1955).

A precipitating factor such as biliary tract disease or a penetrating duodenal ulcer is often evident in acute pancreatitis. This is, however, not the rule and the cause of the attack may remain unclear. The exocrine function may be reduced during the acute attack but when the cause of the inflammatory process is removed the pancreas is restored to normal both functionally and structurally; the development of acute pancreatitis into the chronic form therefore seldom occurs. Calcifications do not develop in acute pancreatitis (HOWAT 1965 SARLES et coll 1965 COOBILL & SOHO 1970 CREUTZFELDT & SCHMIDT 1970 and BANKS 1971). Clinical differentiation between chronic and acute pancreatitis is often impossible due to the fact that the steady progress in the former is interrupted by exacerbations indistinguishable from relapses of acute pancreatitis; only the result in the long term will constitute the deciding factor (AMMAN 1968).

The purpose was to investigate inflammatory pancreatic disease in its various forms and phases in order to understand better the vascular changes demonstrated by angiographic examinations.

Material and Methods

Eighty-seven of the patients (64 males and 23 females) examined by angiography during the period 1960—1971 had inflammatory disease of the pancreas. They were selected by means of the diagnosis established on clinical findings apart from angiography. Consideration was given to the presence of etiologic factors such as biliary tract disease or chronic alcoholism. Symptoms and signs of abdominal pain, jaundice, steatorrhea, diabetes mellitus or gastrointestinal

Table 1

The clinical basis of the diagnosis in the different types of inflammatory pancreatic disease

	Chronic pan- creatitis	Acute pan- creat	Relapsing pan- creatitis
Number of patients	43	28	16
Biliary tract disease	9	12	2
Alcoholism	26	4	7
Reduced exocrine function	29	4	3
Diabetes mellitus	15	2	2
Elev. ted serum or urinary amylase	18	19	16
Operation	30	21	11
Pathology	19	8	6
Pancreatic calcifications	17	—	—

Another three had pathologic glucose tolerance test

Temporary reduction

bleeding were also considered as well as laboratory tests including the analysis of serum or urinary amylase estimation of trypsin in the duodenal content (LUNDH 1962) determination of faecal fat and tests of glucose metabolism. The operation and pathology reports were also evaluated as well as the duration of the condition. Fourteen of the patients previously reported (BORJES & TILLEN 1972) also formed part of the investigation.

Diagnosis. The different types of inflammatory diseases of the pancreas were divided into three groups: chronic pancreatitis, acute pancreatitis and relapsing pancreatitis (Table 1). Decreased exocrine function of the pancreas was considered necessary when selecting patients for the group chronic pancreatitis (AMMAN). However, as the clinical evaluation was usually made in retrospect, data on the exocrine function were not always obtained. Pancreatic calcifications or the pathology findings were therefore also regarded as sufficient (CREUTZFELDT et coll. 1970). A total of 43 patients were thus classified as having chronic pancreatitis based on decreased exocrine function in 29 patients, on the presence of pancreatic calcifications in 7 and on the pathology findings in 7 patients. Diabetes mellitus was present in 15 patients. The glucose metabolism was investigated by glucose tolerance tests in a further 6 patients and was abnormal in 3 of these. Chronic alcoholism was evident in 26 patients. Gall stones were present in 9 patients, in 8 of whom cholecystectomy had previously been performed. Of the others, 22 had normal findings at cholecystography and in 6 of them an additional intravenous cholangiography was also normal. The gall bladder failed to fill in 7 patients, 5 of whom were later explored and proved to

have normal gallbladders. Cholecystography was not performed in 5 patients. Among these latter 12 patients intravenous cholangiography was performed in 8, 5 of whom had normal findings and 3 had dilatation secondary to stenosis of the intrapancreatic part of the common duct.

The group acute pancreatitis comprised 28 patients; the requirement for inclusion in this group was one attack of confirmed pancreatitis. The diagnosis was confirmed by elevation of serum or urinary amylase in 19 patients, 13 of whom were also operated upon. The findings at operation of enlargement and induration of the gland and fat necrosis in the omentum provided the diagnosis in another 8 patients. In one patient temporary decreased exocrine pancreatic function during an attack of abdominal pain established the diagnosis. Decreased exocrine function of the pancreas was recorded in 4 patients. The function had returned to normal at a later examination in 2 patients and in the 2 others the examination was made only a short time after the acute attack when exocrine function is not unusually decreased in all forms of inflammatory disease of the pancreas (LUNDH). Pancreatic calcifications were not demonstrated. Diabetes mellitus was evident in 2 and chronic alcoholism in 4 patients. Trauma was an etiologic factor in 2 other patients and Hodgkin's disease with enlargement of retroperitoneal lymph nodes was present in one patient. This patient developed a pancreatic abscess that required drainage. Biliary tract disease was evident in 12 patients. Cholecystectomy was previously performed in 7 of these, in one of whom stones were also present in the common duct. The gallbladder did not fill in 4 of the remaining patients and stones were demonstrated in the gallbladder in one. Four of these 5 patients have later been operated upon and stones removed and have thereafter had no evidence of pancreatic disease. Cholecystography was normal in 9 patients. In an additional patient the gallbladder was not filled but at operation because of pancreatic abscess; signs of biliary tract disease were not evident.

The third group of 16 patients comprised those with two or more relapsing attacks of pancreatitis. These were in each instance verified by elevation of the urinary or serum amylase values. Since chronic as well as acute pancreatitis may follow a relapsing course, differentiation into these 2 types has not proved practical. The patients however failed to fulfil the criteria of chronic pancreatitis as indicated. Three had moderately decreased exocrine function of the pancreas and were operated upon because of the relapsing attacks and the tail of the pancreas was resected. Pathology in 2 of these patients disclosed slight fibrosis of insufficient degree to permit a diagnosis of chronic pancreatitis; moreover, pancreatography after resection of the tail of the pancreas was normal. In the third patient a duodenal ulcer had penetrated the pancreas. Diabetes mellitus was evident in 2 patients and chronic alcoholism in 7 patients. Cholecystectomy had

been performed before the angiographic examination in 3 patients. In another patient a dysplastic gallbladder was revealed. This patient had been operated upon for duodenal atresia in the neonatal period. Normal findings at cholecystography were recorded in 12 patients. Nonfilling of the gallbladder in one patient was not confirmed at subsequent operation.

Duration. The duration of the condition may influence the angiographic findings as mentioned. It was therefore estimated with due regard to the fact that the onset of abdominal pain is often gradual so that only a crude result is possible. Twenty of the patients in the group of chronic pancreatitis had been affected for more than 5 years, 12 for between 2 and 5 years and 11 for less than 2 years.

The time of onset of the condition in the group of relapsing pancreatitis was more easy to determine as the patients had usually needed hospital care by the first attack. Five patients had had acute phases for more than 5 years, 6 for between 2 and 5 years, and 5 for only 2 years. A more appropriate way to express the duration of this type was to determine the number of attacks demanding hospital admission. 6 patients had had two or three attacks, 5 four or five attacks and 5 patients had had six or more attacks.

Indication for examination. A factor that may also influence the angiographic findings is the indication for the examination which means that if this be performed during an exacerbation, more marked changes may be evident than if carried out during a remission. Analyses disclosed that the purpose of the examination in 15 patients with chronic pancreatitis was a preoperative evaluation during a remission, a search for complications was another common reason. Thus 11 patients had a palpable mass in the abdomen or displacement of the stomach or duodenum revealed by a barium meal. Severe abdominal pain possibly attributable to carcinoma of the pancreas was the indication for angiography in 12 patients and 3 were examined because of jaundice. In 2 patients, previous operation following nonfilling of the gallbladder at cholecystography disclosed hard induration and enlargement of the head of the pancreas, angiography was performed to confirm the operative diagnosis of chronic pancreatitis.

The main reason for the examinations in the group of acute pancreatitis was also complications. Thus, 12 patients were examined because of a palpable mass or displacement of the stomach or duodenum disclosed by a barium meal. Two patients underwent angiography because of persistently elevated serum amylase levels after an acute attack of pancreatitis and after cholecystectomy respectively. Other reasons for examination were the findings at operation in 3 patients of acute hemorrhagic pancreatitis, pancreatic abscess and induration of the head of the pancreas respectively. Other indications for angiography were jaundice

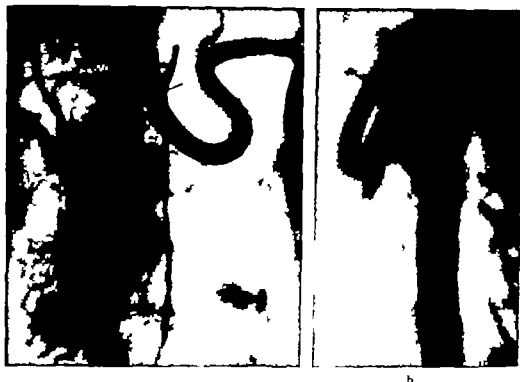


Fig. 1. Woman, aged 64, with calcifying chronic pancreatitis for many years. a) Spasm in the first part of the splenic artery (—) Short stenosis at the origin of the gastroduodenal artery (---). The pancreaticoduodenal vessels (↔) are tortuous and dilated. The head of the pancreas is hypervascularized with tortuous and slightly irregular vessels. b) Aortic injection. Lateral projection. Complete stenosis of the superior mesenteric artery and marked stenosis of the coeliac artery. Collateral circulation from the inferior mesenteric artery and the middle colic artery.

in 2, melena in 1 and trauma in 1 patient. In the remaining 7 patients severe abdominal pain was the reason for the angiographic examination.

In the group of relapsing pancreatitis, 3 patients had a palpable mass in the upper abdomen as the indication for angiography. The other 13 were examined as part of a preoperative evaluation and search for precipitating factors.

The vascular changes in the three different types of inflammatory pancreatic disease were analyzed separately. It was assumed that as pancreatitis often advances the vascular changes might also be progressive and they were therefore correlated to the duration of the disease. Finally, special variants such as calcifying chronic pancreatitis, pancreatitis secondary to biliary tract disease or pancreatitis complicated by pseudocyst and abscess were also investigated.



Fig 2 Male aged 41 alcoholic with chronic pancreat us Smooth regular stenosis in the splenic artery The arteries in the tail of the pancreas are irregular



b

Fig 3 Male aged 42 alcohol with chronic pancreat us a) Slight smooth stenosis of the splenic artery (—) Saccular changes in the wide pancreatic arcades (—) Hypovascularization of the body and tail of the pancreas b) The stenosis changes the splenic artery accentuated (—) after 10 μ g of norepinephrine in the coeliac artery

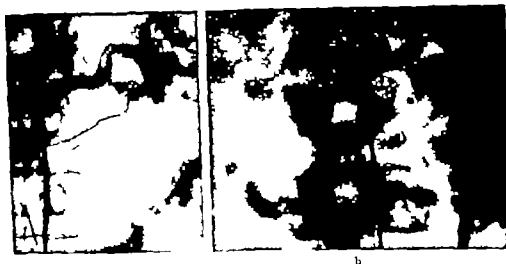


Fig. 1. Woman, aged 64, with calcifying chronic pancreatitis for many years. a) Spasm in the first part of the splenic artery (→). Short stenosis at the origin of the gastroduodenal artery (⊔→). The pancreatic arcades (↔) are tortuous and wide. The head of the pancreas is hypervascularized with tortuous and slightly irregular vessels. b) Aortic injection. Lateral projection. Complete stenosis of the superior mesenteric artery and marked stenosis of the coeliac artery. Collateral circulation from the inferior mesenteric artery and the middle colic artery.

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b

Fig 5 Male aged 52 alcohol with calcifying pancreatitis a) Wide dorsal pancreatic artery (—) giving off the tortuous transverse pancreatic artery (I—) The branches in the tail of the pancreas are irregular b) Thromboses of the splenic vein Collateral circulation through gastroduodenal and coronary veins (H—)

this artery with collateral circulation from the inferior mesenteric artery via the middle colic artery (Fig 1) in the remaining patient, isolated stenosis of the superior mesenteric artery was present Arterial aneurysms were recorded in 4 patients in the gastroduodenal artery in 2 and in the splenic in 2 patients one of these also had an aneurysm of a jejunal artery The most common finding in creased tortuosity of the pancreatic arcades and intrapancreatic arteries, was present in 38 patients in 24 of these the tortuosity was combined with slight irregularity of the lumen (Figs 2 4 5) Changes in the middle colic artery were present in 12 patients (Fig 4) these consisting of increased tortuosity and sometimes slight irregularity of the arterial lumen Changes in the jejunal arteries were recorded in 4 patients

The vascularization of the pancreas was regarded as increased in 18 and decreased in 15 patients in one patient the vascularization was enormously increased and arteriovenous shunting was evident (Fig 6) This was the only patient in whom pancreatic veins were demonstrated

Displacement of arteries caused by an abscess or a pseudocyst was present in 6 patients In another 4 patients the whole pancreas together with the gastroduodenal artery and the pancreatic arcades were markedly displaced to the left The cause of this was thought to be retroperitoneal adhesions The arcades were stretched by the mere enlargement of the head of the pancreas in 4 patients One patient had displacement of intestinal arteries probably due to adhesions

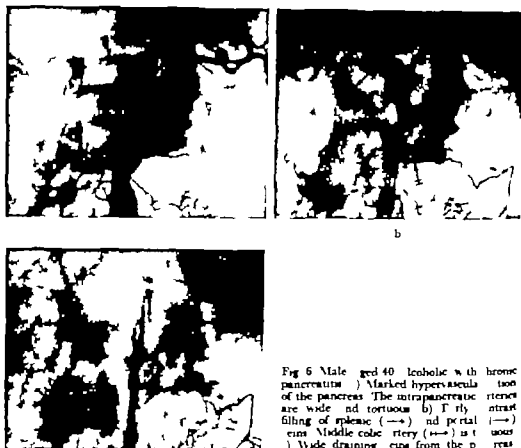


Fig 6 Male aged 40 alcoholic with chronic pancreatitis. a) Marked hypervascularity of the pancreas. The intrapancreatic arteries are wide and tortuous. b) Early contrast filling of splenic (—→) and portal (—→) veins. Middle colic artery (—→) is tortuous. c) Wide draining vein from the pancreas.

Changes in the splenic vein were present in 23 patients. These consisted of compression in 7 and occlusion in 16 patients (Fig 5). In only one patient was the vein displaced without signs of any other lesion. The superior mesenteric vein was compressed in 6 and the portal vein in 3 of these patients. A combination of a lesion of the splenic artery and vein was present in 15 patients. The incidence of superior mesenteric vein involvement might possibly have been even higher as it could not be evaluated in 8 patients, due to low concentration of contrast medium in 7 and the fact that the superior mesenteric artery was not injected in one patient (Table 2).

The vascular changes related to the duration of the disease revealed an increasing frequency of tortuousity and lumen irregularities of the pancreatic arteries in patients with longstanding disease. Stenotic arterial changes were about as common but tended to extend to more arteries with increasing duration. The

Table 2

Vascular changes at angiography in different types of inflammatory pancreatic disease

	No	Arteries					Veins			
		Stenosis of extra-pancreatic art.		Transparen-ent art.		Displacement				
		1	> 2	Tortu-ous	Irreg-ular lumen	Extra-pancr	Paper	Com-pression	Occlu-sion	
Chronic pancreat-itis	43	14	10	12	38	24	6	8	7	16
Acute pancreat-itis	28	6	5	7	22	10	8	1	10	4
Relapsing pancreat-itis	16	8	1	3	10	6	3	3	3	3
Pseudocyst or abscess	21	8	6	6	18	14	16	2	9*	7

Further 11 patients had only displacement of veins

Table 3

Progress of vascular changes in chronic pancreatitis in relation to duration of disease

Duration	No	Number of extrapancreatic arteries with stenotic channels			Extension of venous lesions			
		1	2	> 2	Splenic vein	Superior mesenteric vein	Portal vein	
Less than 2 years	11	4	3	1	2	4	—	—
2 to 5 years	12	4	3	4	3	4	2	—
More than 5 years	20	6	4	7	2	8	4	3

frequency and extension of venous lesions markedly increased with time. Thus lesions of the superior mesenteric vein were not evident unless the patient had been ill for more than 2 years and changes in the portal vein were demonstrated only in patients with disease of more than 5 years duration (Table 3).

Calcifications of the pancreas were present in 17 patients (Figs 1-5) all with the disease for more than 2 years, and 11 of them for more than 5 years. In this separate group vascular changes occurred about as often as in noncalcifying chronic pancreatitis of the same duration. The vascularization of the pancreas, however, was more often reduced in patients with calcifications than in those

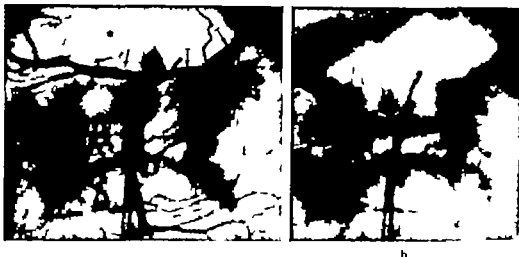


Fig 7 Female aged 66 with abdominal pain for few months. Palpable tumor in epigastrium. Later operation disclosed pseudocyst. a) Smooth regular tapering stenosis of the common hepatic (→) and splenic (⇨) arteries. Gastroduodenal artery (⇨⇨) is stenosed and laterally displaced. b) Compression of the celiac axis in the confluence.

without, and this difference was accentuated the longer the duration of the disease. No aneurysms, pseudocysts or abscesses were recorded.

Acute pancreatitis. All the 28 patients in this group underwent examination of the coeliac artery and 24 of the superior mesenteric artery. A smooth contraction around the tip of the catheter caused by spasm was evident in one patient. Stenotic arterial changes were recorded in 18 patients (Fig 7), these being most often located in the splenic artery (12), the common hepatic artery (11) and the gastroduodenal artery (9 patients). Vasoconstrictive agents were given to 19 patients and accentuated the stenosis in one patient. Changes of the fibromuscular dysplasia type were demonstrated in 1 patient, who also had other stenotic arterial changes. The coeliac artery was stenosed in 10 patients, 3 of whom had stenosis of the superior mesenteric artery as well. An arterial aneurysm of the splenic artery was present in 2 patients, one of whom also had an aneurysm of the gastroduodenal artery. In addition, aneurysmal dilatations of the coeliac and common hepatic arteries were evident in one patient (Fig 8). Tortuous vessels in the pancreas were noted in 22 patients, in 10 with lumen irregularities, narrowing and widening (Figs 9, 10). Increased tortuosity of the middle colic artery was demonstrated in 7 patients and 2 patients had changes in the small intestinal arteries, one in the jejunal and one in the jejunal and ileal arteries. The vascularization of the pancreas was increased in 8 (Fig 7) and decreased in 5 patients. Displacement of arteries was recorded in 9 patients, being caused by

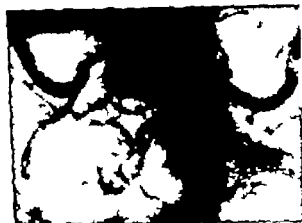


Fig 8 Male, aged 63 with track of pancreatitis one and half year previously. Note when intermittent abdominal pain. Aneurysm of coelia (\rightarrow) and common hepatic (\rightarrow) arteries with narrowing of the common hepatic artery distal to the aneurysm. Collateral circulation through dorsal pancreatic artery (\leftrightarrow)

a pseudocyst or an abscess in 8 of these (Fig 10). In one patient the whole pancreas together with the gastroduodenal artery and the arcades were displaced to the left.

The splenic vein was affected in 15 patients by compression in 10 and occlusion in 4 patients; mere displacement was evident in only one instance. Compression of the portal vein was present in one patient with a pseudocyst (Fig 7). The superior mesenteric vein was not demonstrated in 5 patients and consequently the incidence of lesions involving this vein is possibly underrated. Lesions of the splenic artery and vein in combination were observed in 9 patients (Table 2).

Biliary tract disease was regarded as a possible cause of the pancreatitis in 9 patients. Stones in the common duct were subsequently removed at operation in 2 of these patients; the others having stones in the gallbladder. One patient was examined for pancreatic abscess and 2 other patients for pancreatitis complicating cholecystectomy. The vascular changes in these patients differed little from those in patients without concomitant biliary tract disease.

Relapsing pancreatitis. The 16 patients in this group underwent examination of the coeliac artery and 15 patients of the superior mesenteric artery as well. Spasm around the tip of the catheter was recorded in 7 and stenotic arterial changes were present in 10 patients (Fig 11). The localization was the splenic artery in 7 patients; the gastroduodenal in 3 and the common hepatic artery in 3 patients. Vasoconstrictive agents were used at the examination in 13 patients, and the stenotic changes were accentuated in 3 patients. Changes suggesting fibromuscular dysplasia were evident in one patient. Stenosis of the coeliac artery was not demonstrated but one patient had stenosis of the superior mesenteric artery. Aneurysm of the splenic artery was present in one patient. The pan-

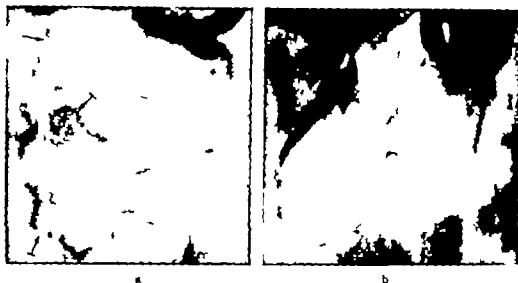


Fig 9 Female aged 59 with pancreatic abscess drained 3 weeks previously. a) Tightening smooth stenosis of the gastroduodenal artery (—→) Pancreatic arcade (|—→) and intrapancreatic arteries are wide, tortuous and irregular. b) One year later. Normal width of the arcade. The tortuosity has disappeared. Intrapancreatic arteries are still slightly irregular.

creatic arteries were tortuous in 10 patients, in 6 of whom they also displayed a slightly varying lumen (Fig 11). The middle colic artery was tortuous and slightly irregular in 4 patients (Fig 12). The vascularization of the pancreas was increased in 5 and decreased in 6 patients. Six patients had involvement of the splenic vein with compression in 3 and occlusion in 3 (Fig 12), while one patient had compression of the superior mesenteric vein. Displacement of the pancreatic arcades due to enlargement of the head of the pancreas was present in 2 patients. In one patient the whole pancreas and the gastroduodenal artery were displaced to the left, possibly because of retroperitoneal adhesions (Fig 12). In 3 patients vascular displacement resulted from a pseudocyst or an abscess (Table 2).

The vascular changes increased in relation to the duration of the disease, but this was even more obvious if correlation were made to the number of attacks. The most marked increase was in venous lesions. However, the frequency of stenotic changes in arteries surrounding the pancreas and of tortuosity and lumen irregularities in pancreatic arteries also increased (Table 4).

Pseudocyst and abscess Expansive lesions of the pancreas were recorded in 21 patients: 10 pseudocysts and 11 abscesses; only one abscess was evident among the patients with the disease for more than 2 years. Abscesses complicated acute in 6, chronic in 3, as well as relapsing pancreatitis in 2 patients. The pseudocysts

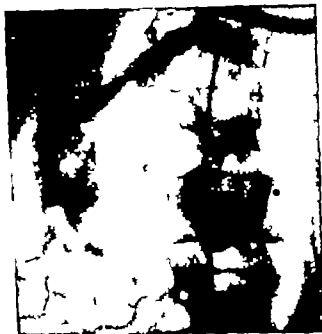


Fig 10 Female aged 57 with acute pancreatitis 3 months previously. Displacement of the stomach (barium meal examination). Operation disclosed pancreatic abscess. Displacement of the splenic and gastroduodenal arteries. Pancreatic arcades stretched and filled with typical alternating narrowings and dilations (\rightarrow). The transverse pancreatic artery (\dashrightarrow) is irregular.

were demonstrated in patients with chronic and relapsing pancreatitis 5 of whom had disease of more than 5 years duration and 2 for between 2 and 5 years. The remaining 3 pseudocysts occurred in patients with acute pancreatitis.

Displacement of arteries was recorded in 17 patients (Figs 7-10). The diagnosis was difficult in those patients in whom no displacement could be demonstrated. In one patient with acute hemorrhagic pancreatitis extensive changes in the pancreatic as well as intestinal arteries were evident and a retroperitoneal abscess was therefore not diagnosed before operation. In another patient only hypovascularization corresponding to pseudocystic degeneration of the pancreatic tail was present. Compression of the veins in 2 patients was the only evidence of an expansive lesion of the pancreas.

Arterial stenotic changes were registered in 20 patients and the pancreatic arteries were tortuous in 18, in 14 of whom they had also a varying, slightly irregular lumen (Fig 10). Lesion of the intestinal arteries, mainly the middle colic artery, was recorded in 10 patients. Eighteen patients had venous lesions (Fig 7).

An attempt to differentiate between a pseudocyst and an abscess by angiography alone disclosed only minor differences. Changes in the intestinal arteries were more common in pancreatic abscess although differentiation was not possible from these alone.



Fig 11 Male aged 58 with relapsing pancreatitis. Examination after 10 μ g of norepinephrine into celiac artery. Mild smooth stenosis of the splenic artery (—>). Regularly varying lumen of the transverse pancreatic artery (==>).

Discussion

Disagreement exists concerning the vascular changes in inflammatory pancreatic disease as investigated by angiography. This may be due to the fact that most reports have been based on experience in only a few patients in whom no particular effort was made to correlate the angiographic findings with the type and stage of the disease (BAUM *et coll* 1965, ROSCH & BREIT 1965, NEDESR & POLLARD 1967, SAMMONS *et coll* 1967, MOSKOWITZ *et coll* 1968, BUCHSLEIN *et coll* 1971, LECHEMER & FORJESER 1971).

The different types of inflammatory pancreatic disease mentioned formed the basis for the grouping of the patients in this material. Since the borders between the clinical groups are not sharp and elaborate methods are necessary to separate the patients it has not been practical to extend the differentiation further especially as the evaluation has usually been made in retrospect.

Arterial stenosis of different morphologic types has been described in pancreatitis (HERNANDEZ *et coll* 1967, MOSKOWITZ *et coll* 1968). It has, however, also been pointed out that this is nonspecific and difficult to differentiate from atheromatosis and fibromuscular dysplasia (REUTER *et coll* 1969). The vascular changes may increase in progressive disease but may decrease if the pathologic process be halted or slowed down, for example by operation (BOIJSEN & TILLEN 1972). The causes of the changes may be postinflammatory fibrous adhesions



Fig 12 Male aged 51 with relapsing pancreatitis previously operated upon for pseudocyst. Later operation disclosed penetrating duodenal ulcer. a) Displacement of the gastroduodenal artery (\rightarrow) to the left. Tortuous transverse pancreatic (\rightarrow) and middle colic (\leftrightarrow) arteries. b) Compression of the celiac with collateral circulation.

or involvement of the lymphatic system (BOJSEN 1971). Another explanation may be that the increased irritability of the arterial wall initiated by the inflammatory process may increase the tendency of the hypertonic contrast medium to cause spasm. This theory is supported by a frequent occurrence of short membrane like contractions around the tip of the catheter during the injection (HERNANDEZ et coll.). Arterial spasm at the tip of the catheter was common in the present material (Fig 1). Many instances of smooth regular stenotic changes in the arteries surrounding the pancreas were recorded in patients belonging to all three groups (Figs 2, 3, 7, 11) although more common in chronic pancreatitis (Table 2). The changes were in some patients enhanced by the injection of vasoconstrictive agents (Fig 3) which further supports the theory of spasm. A similar reaction has been reported in conjunction with the malignant encasement of vessels in carcinoma of the pancreas (KAUDZ & WIRTANEN 1970).

An increase in the number of stenotic arterial changes in patients with disease of more than 2 years duration has been reported (REUTER et coll 1969) these were even more accentuated among the present patients with disease for more than 5 years. A close correlation to the number of relapsing attacks also existed (Table 4).

Celiac artery stenosis apparently is found more often in pancreatitis (BUCHLER et coll 1971, LECHNER & POMERER 1971). However 12.5 per cent of

Table 4

Vascular changes in relapsing pancreatitis related to number of attacks

	Number of attacks		
	2 to 3	4 to 5	6 or more
N. of patient	6	5	3
Stenotic arterial changes	3	4	3
Tortuous pancreatic arteries	4	3	3
Irregular lumen of pancreatic arteries	1	1	4
Venous lesion	2	2	3

patients examined by angiography for unrelated disease had coeliac artery stenosis and 3.4 per cent superior mesenteric stenosis (BROU & REDMAN 1969) even higher figures have been recorded at autopsy of patients without pancreatic disease (DERPICK *et coll* 1959). Stenosis of the coeliac artery was observed in 16 of the present patients and of the superior mesenteric artery in 9 patients. Combined lesions were present in 7 patients (Fig. 1). The value of these findings is uncertain and further work on the problem is needed. Two opposite views are offered: (1) Ischemia may result from coeliac and superior mesenteric artery stenosis. This is highly improbable as a cause of pancreatitis considering the abundant collateral circulation in the abdomen (MICHAELS 1969, REUTER 1970). (2) As stenotic changes of the arteries surrounding the pancreas caused by the inflammatory process are common the condition may as well cause stenosis of the coeliac artery and especially of the superior mesenteric artery with its intimate relation to the uncinate process of the pancreas.

Changes in the intrapancreatic arteries consisting of increased tortuosity and lumen irregularities giving the arteries a beaded appearance have been regarded as typical of pancreatitis (REUTER *et coll*, BOJSEN & TYLÉN). The changes consist of thickening of the media and subintimal fibrosis of the small arteries with narrowing of the lumina (HOWARD & NEDWICK 1971). The highest incidence of such changes was observed among the present patients with chronic pancreatitis of more than 5 years duration with the exception however of those with calcifying chronic pancreatitis. The hypovascularization was marked in the latter which may explain the finding. The vascular changes were also common in patients who had 6 or more relapsing attacks of pancreatitis (Table 4, Fig. 11). More increased tortuosity of pancreatic vessels was evident in 38 patients with chronic pancreatitis in 22 with acute and in 10 patients with relapsing pan-

creatitis this being the most common finding of all. The changes may develop during an attack, but are reversible and leave some permanent scarring (Fig 9).

Arterial aneurysms are often present in pancreatitis and the risk of rupture has previously been pointed out (HADJILL & RILEY 1967; BOIJSEN *et coll* 1969; GAUTIER-BENOIT *et coll* 1970); their demonstration in 8 patients (9 per cent) of the present material further stresses the fact (Fig 8). Aneurysms were equally frequent in the different types of inflammation and were not more common in longstanding disease. On the other hand no aneurysm was recorded among the patients with calcifying chronic pancreatitis even with marked vascular changes; neither were there abscesses nor pseudocysts. This might correspond to the fact that this type of disease has less tendency to necrosis (SAPLES *et coll* 1965). Progressive arterial changes with increased tortuosity and an irregular lumen have been reported in the middle colic artery in chronic pancreatitis (BOIJSEN & TYLEN). Similar changes were evident in the present patients with chronic as well as with acute and relapsing pancreatitis (Figs 6-12) although they were more common in the chronic group. Lesions of small intestinal arteries in acute pancreatitis have been reported (COLLINS *et coll* 1968; GRIFFITHS & BROWN 1970). Small intestinal arteries were affected in 6 instances in the present series of patients. The changes in one patient with acute hemorrhagic pancreatitis extended down the main stem of the superior mesenteric artery and also appeared in the ileal and the ileocolic arteries; operation disclosed intense inflammatory reaction of the distal part of the small intestine and necrosis of the ascending colon (TYLEN & DENCKER 1973).

Previous investigations have been contradictory in the evaluation of the vascularization of the pancreas in inflammatory disease. Both hypervascularization (ROSCHE & BREY) as well as extreme hypovascularization (HERNANDEZ *et coll*) have been reported. The differences may in part be explained by variations in technique but the fact that different types of pancreatitis exist and that the examinations may have been performed at various stages of the disease must also be taken into consideration. No typical changes with the exception of extreme hypovascularization in calcifying chronic pancreatitis could be defined in the present series. Complete avascularity as reported by HERNANDEZ *et coll* was however not encountered. One patient had extreme hypervascularization and arteriovenous shunting (Fig 6) and was operated upon and the body and tail of the pancreas resected; pathology failed to establish the cause of the condition.

Venous lesions in pancreatitis are common (ROSCHE & BREY; REUTER *et coll*; LECHNER & POKIESER; BOIJSEN & TYLEN). The large visceral veins pass close to the pancreas with the splenic vein running along the cranial and dorsal aspect of the body and tail. The thin walls of the veins make them particularly vulnerable. Venous lesions were recorded in about 50 per cent of the patients; the incidence

was about the same in the different types of pancreatitis but rose in relation to the duration in chronic pancreatitis (Table 3) while compression was more common in acute and in relapsing pancreatitis and occlusion occurred more often in chronic pancreatitis (Table 2, Figs 5-7, 12). Combined lesions of the splenic artery and vein have been said to suggest pancreatic carcinoma (NEBELAR & POLLARD BUCHLER *et coll.*) it appears to be even more common in pancreatitis (Fig 5).

The necessity of observing the phase of the disease at the time of examination is stressed: one group of patients with acute pancreatitis and elevated urinary amylase levels was examined in the early acute phase (AARHUS *et coll.* 1969). There was a slight enlargement of the pancreas and some increase of the width of the arteries, apparent only when compared with the angiography performed a few months later. The patients in the present investigation with acute pancreatitis differ from those of AARHUS *et coll.* in that the examinations in the former were not performed in the early acute phase, but only after complications had supervened: this possibly explains the often marked changes. The patients with relapsing attacks were on the other hand usually examined during a remission and the changes were less marked, even if they became more prominent with a greater number of attacks and a longer duration of the condition.

Comparison of the angiographic findings in patients with and without increased serum amylase levels and without regard to the stage of the disease have also been made (REUTER *et coll.* BUCHLER *et coll.*) The elevation of the serum amylase is of short duration and may not be detected: it is not strongly correlated to the severity of the inflammatory process (DIACO *et coll.* 1970). Moreover an exacerbation of chronic pancreatitis may pass without elevation if destruction of the parenchyma has progressed far enough. Estimation of the amylase level is therefore not sufficient as an indicator of the activity of the disease and a more elaborate investigation is necessary to distinguish different types of inflammatory pancreatic disease (AMMAN 1968).

HERNANDEZ *et coll.* and REUTER *et coll.* failed to observe vascular changes in 10 and 22 per cent, respectively, of patients with pancreatitis. Only 2 of the present patients had normal findings: one patient had had a single attack and one had previous relapsing attacks: both were operated upon. In the former patient only slight induration of the head of the pancreas was evident and in the latter in whom the tail of the pancreas was resected only slight lipomatoses.

The vascular changes in pancreatitis secondary to biliary tract disease differed little from those in pancreatitis of the same duration, but without biliary tract disease. The changes may be marked however and in one patient with stones in the common duct, changes that could not be differentiated from those of long standing chronic pancreatitis were present.

Necrosis may occur as a complication of all the different types of pancreatitis. An abscess or a pseudocyst may then develop (ALTMAYER & ALEXANDER 1964; STEEDMAN et coll 1967; BOLOOKI et coll 1968; EVANS 1969). The angiographic diagnosis of pseudocysts of the pancreas on record is based on displacement of arteries, pressure changes upon arteries and hypovascularization in the region of the pseudocyst (HERNANDEZ et coll; RUTTER et coll; ROSEN & BRIET). The findings in pancreatic abscess are similar (TILLY & DENCKER). Displacement of vessels was a common finding in pseudocyst as well as in abscess in the present material (Figs 7-10). Depending on the localization and size of the expansive lesion the diagnosis may be impossible if the vascular displacement be only moderate. Small expansive lesions in the region of the body and tail of the pancreas are thus especially difficult to diagnose as these parts are not so well delineated by large vessels as is the head. Extreme hypovascularity of such a lesion may facilitate the diagnosis and often extend into the lesser omental sac or mesocolon when displacement of the left gastric and middle colic arteries, respectively, occurs. This finding may help in arriving at the diagnosis. Compression or occlusion of the veins close to the pancreas was also a common finding, and in 2 patients was the only one suggesting the diagnosis in the absence of displaced vessels. Stenotic arterial changes corresponding to the type and phase of the disease were also evident in all patients with expansive lesions. The differentiation between pseudocyst and pancreatic abscess by angiography alone was impossible. The clinical course is however different and should allow differentiation as soon as the pancreatic origin of the disease is established.

A particular type of arterial displacement was registered in 6 patients. The whole pancreas together with the gastroduodenal artery and the pancreatic arcades were displaced towards the left (Fig. 12). This corresponded to the intense fibrous scarring of the retroperitoneal space, common in the course of progressive inflammatory disease of the pancreas. It was verified at operation in 5 of the patients; in the sixth patient operated upon several months after angiography no fibrosis was discovered, a possible explanation being displacement due to a pseudocyst that at the time of operation had disappeared.

Differential diagnosis. The vascular changes in pancreatitis appear to be characteristic but not pathognomonic. The angiographic findings may therefore sometimes suggest the diagnosis. The frequency of a false positive diagnosis made in this way is impossible to determine as the true condition will often not be disclosed by surgery or pathology. Retroperitoneal tumours such as reticulum cell sarcoma, lymphosarcoma and lymph gland metastases may cause displacement and stenotic changes of the arteries surrounding the pancreas like a pancreatic pseudocyst. Lesions of veins may also be evident. Changes in the intrapancreatic arteries have, however, not been observed. Pancreatitis was suggested in a few

patients examined for jaundice or a palpable abdominal tumour later operation revealed cholecystitis and the pancreas was normal at palpation. These patients had stenotic arterial changes and hypervascularization. The diagnosis was made on the basis of aneurysms in the gastroduodenal and splenic arteries in two other patients, respectively. At operation the pancreas was normal. Marked stenotic arterial changes like those in pancreatitis were also present in one patient examined during hypovolemic shock from a bleeding gastric ulcer. No signs of pancreatitis were evident post mortem. The changes were probably caused by vascular spasm initiated by released vasoconstrictive substances. Similar stenotic changes were also demonstrated in one patient in whom at autopsy the pancreas was normal; these may have been caused by atheromatosis. Finally the diagnosis of pancreatitis was made angiographically on the basis of mere hypervascularization. A few of these patients had stenosis of the coeliac artery with collateral circulation through and around the pancreas; however they were not operated upon and the findings were not verified.

These difficulties in the differential diagnosis have all been due to the fact that only changes in vessels surrounding the pancreas have been considered. In no instance were there changes in the intrapancreatic arteries which thus seems to be the only finding characteristic of pancreatitis.

A few patients were proved at operation to have carcinoma of the pancreas. This will be reported in another paper (TYLEN to be published).

Conclusions

Vascular changes in vessels within the pancreas and surrounding it regularly occur in inflammatory pancreatic disease. The changes in the arteries surrounding the pancreas consist of slight smooth, regular stenosis over a segment of varying length; they may sometimes be accentuated by vasoconstrictive agents and arterial spasm may occur at the tip of the catheter as the contrast medium is injected. Arterial aneurysms are also common. The changes in the intrapancreatic arteries consist of increased tortuosity and a slightly irregular lumen and sometimes a beaded appearance. Changes in the intrapancreatic arteries are the only ones not occurring in other diseases, and may therefore be regarded as being associated with inflammatory disease. Similar changes are common in the intestinal arteries mainly the middle colic artery. The large veins adjacent to the pancreas are often affected; about half of the patients had compression or occlusion of the veins. Pancreatic vascularization varies in appearance and except for progressive hypovascularization in calcifying chronic pancreatitis, cannot be correlated directly to a certain type or phase of disease.

These types of changes are demonstrated in all forms of chronic, acute and relapsing pancreatitis and increase in degree and extension with the duration in chronic pancreatitis and with the number of relapsing attacks. They may be as marked and extensive in acute as in long standing chronic pancreatitis if the patient is examined during a prolonged and complicated course of the disease. On the other hand they may be less marked in relapsing attacks if the examination be performed during a remission. It is therefore probable that vascular changes developed during the acute phase are reversible in uncomplicated conditions with a raised number of relapsing attacks and increasing duration. However the changes may not be fully reversed.

The diagnosis is mainly based on vascular displacement in pancreatic pseudocysts or abscess. Other types of vascular changes corresponding to the type and phase of disease are also evident.

This investigation suggests that the high incidence of complications such as aneurysm, venous occlusion and expansive lesions are indications for angiographic evaluation as soon as surgical treatment is contemplated in inflammatory disease of the pancreas. When evaluating the angiographic findings consideration of the type and phase of disease is of the utmost importance.

Acknowledgement

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SUMMARY

Fifty seven patients with inflammatory disease of the pancreas were investigated by angiography. A high incidence of arterial and venous changes was evident and these were similar in the different types although more marked in the complicated conditions and in those of long duration. The common complications of arterial aneurysms, pseudocysts and venous occlusion are discussed.

ZUSAMMENFASSUNG

Sebenundachtzig Patienten mit entzündlichen Erkrankungen des Pankreas wurden angiographisch untersucht. Arterielle und venöse Veränderungen wurden häufig beobachtet und waren gleichartig in den verschiedenen Typen obwohl ausgeprägter in den komplizierten und lang anhaltenden Fällen. Gewöhnliche Komplikationen wie arterielle Aneurysmen, Pseudokysten und Venenocclusion werden diskutiert.

RÉSUMÉ

Quatre-vingt-sept malades atteints d'affection inflammatoire du pancréas ont été examinés par angiographie. Les modifications veineuses et artérielles étaient très fréquentes et elles étaient semblables dans les différents types bien que plus marquées dans des affections compliquées et les affections de longue durée. Les auteurs étudient les complications fréquentes d'anévrismes artériels, de pseudokystes et d'occlusion veineuse.

REFERENCES

- AARHUS T, HOFSLI M and VESTAD E. Angiography in acute pancreatitis. *Acta radiol. Diagnosis* 8 (1969) 119.
- ALTEMEYER W A and ALEXANDER J W. Pancreatic abscess. *Arch Surg* 87 (1963) 80.
- AMMAN R. Die Differentialdiagnose zwischen akut reversibler und chronisch progressiver Pancreatitis. *Schweiz med Wochr* 90 (1968) 744.
- BAKIS P A. Acute pancreatitis. *Gastroenterology* 61 (1971) 382.
- BALM S, ROY R, FINKELSTEIN A K and BLACKMORE W S. Clinical application of selective coeliac and superior mesenteric arteriography. *Radiology* 84 (1965) 279.
- BOISEN E. Angiography in pancreatic disease. *Acta gastro-ent belg* 33 (1970) 391.
- Pancreatic angiography. I. Angiography. Second edition. Edited by H L Abrams. Little Brown and Company Boston 1971.
- GOTTLIN J, HALLBOOK T and SANDBLÖM P. Preoperative angiographic diagnosis of bleeding aneurysms of abdominal arteries. *Radiology* 93 (1969) 781.
- and TYLEN U. Vascular changes in chronic pancreatitis. *Acta radiol. Diagnosis* 12 (1972) 34.
- BOLOOKE H, JAFFE B and GLIEDMAN M L. Pancreatic abscesses and lesser sac collections. *Surg Gynec Obstet* 126 (1968) 1301.
- BOONSTEIN J J, REUTER S R and MARTEL W. Angiographic evaluation of pancreatic carcinoma. *Radiology* 93 (1969) 737.
- BROWN K M and REDMAN H C. Splanchnic artery stenosis and occlusion. *Radiology* 92 (1969) 323.
- BUCHLER E, BOLDT I, FROMMHOFT H and KAUFER C. Die angiographische Diagnostik der Pankrestumoren und der Pancreatitis. *Fortschr Röntgenstr* 115 (1971) 726.
- COOBBILL C L and SONO H. T. Acute pancreatitis. *Arch Surg* 100 (1970) 673.
- COLLINS J J, PETERSON L M and WILSON R E. Small intestinal infarction as a complication of pancreatitis. *Ann Surg* 167 (1968) 433.
- COMFORT M W, GAMMILL E F and BAGGISTON A H. Chronic relapsing pancreatitis: a study of 29 cases without associated disease of the biliary or gastrointestinal tract. *Gastroenterology* 6 (1946) 239-376.
- CREUTZFELDT W and SCHMIDT H. Aetiology and pathogenesis of pancreatitis. *Scand J Gastroent* (1970) Suppl No 6 p 47.
- FRIED H and SCHMIDT H. Verlaufsbeobachtungen und diagnostische Verfahren bei der chronisch rezidivierenden und chronischen Pancreatitis. *Schweiz med Wochr* 100 (1970) 1180.
- DERRICK J R, POLLARD H S and MOORE R M. The pattern of arteriosclerotic stenosis of the coeliac and superior mesenteric arteries. *Ann Surg* 149 (1959) 684.
- DIACO J F, MILLER L D and CORLEAND E M. The role of early diagnostic laparotomy in acute pancreatitis. *Surg Gynec Obstet* 129 (1970) 263.
- DIXON J A and ENGLERT E. Growing role of early surgery in chronic pancreatitis: a practical clinical approach. *Gastroenterology* 61 (1971) 375.
- F AND F G. Pancreatic abscess. *Arch Surg* 117 (1969) 337.
- FITZGERALD O, FITZGERALD P, FEENELEY J, McMILLIN J P and BOLAND S J. A clinical study of chronic relapsing pancreatitis. *Gut* 4 (1963) 193.
- GAUTIER-BENOIT C, LERU J, LHERMINIER CL, PARIS J CL, WURTZ A et MORTIER J. Rupture artérielle au cours de l'évolution des pseudokystes pancréatiques. *Ann Chir* 24 (1970) 907.

- GRIFITHS R W and BROWN P W Jejunal infarction as a complication of pancreatitis *Gastroenterology* 58 (1970) 709
- HERNANDEZ CL ECARLAT B et BERNUTH V L'artériographie des affections pancréatiques *J Radiol* 48 (1967) 327
- HOWARD J M and NEDOVICK A Correlation of the histologic observations and operative findings in patients with chronic pancreatitis *Surg Gynec Obstet* 132 (1971) 387
- HOWAT H T Chronic pancreatitis *Bibl gastroent* 7 (1965) 31
- KADILL B M and RILEY J M Major arterial involvement by pancreatic pseudocyst *Amer J Roentgenol* 99 (1967) 632
- KAUDE J V and WERTAMER G W Celiac epinephrine enhanced angiography *Amer J Roentgenol* 110 (1970) 818
- LACERRE G and POISSIER H Ergebnisse angiographischer Untersuchungen bei Pankreatum *Fortschr Röntgenstr* 114 (1971) 49
- — ZACHARIAS W und BELCHER P Zur angiographischen Diagnose des Pankreasleidens *Fortschr Röntgenstr* 113 (1970) 340
- LEVYAT M DUBON L MOULVIER B et PASQUIER J Evolution au long cours des pancréatites chroniques *Arch Mal Appar dig* 59 (1970) 5
- LYONS G Pancreatic exocrine function in neoplastic and inflammatory disease: a reliable and simple new test *Gastroenterology* 42 (1962) 275
- LUNDENQUIST A Angiography in carcinoma of the pancreas *Acta radiol* (1965) Suppl No 235
- MICHAELS N A Blood supply and anatomy of the upper abdominal organs *J B Lippincott Philadelphia and Montreal* 1969
- MORLOWITZ H CHAIT A and MELLING H Z Tumour encasement of the coeliac axis due to chronic pancreatitis *Amer J Roentgenol* 104 (1968) 641
- NIEBERER R A and POLLARD J J A critical evaluation of coeliac and superior mesenteric angiography in the diagnosis of pancreatic disease particularly malignant tumour: facts and artefacts *Radiology* 89 (1967) 1017
- OLSON O Angiography in tumours of the pancreas *J Modern trends in diagnostic radiology* p 190 Edited by J W McLaren Butterworths London 1970
- RANDWIGER B and SALERNO R M Arteriographic diagnosis of pancreatic lesions *Radiology* 85 (1966) 470
- REUTHER S R Modification of the pancreatic blood flow with balloon catheters: A new approach of pancreatic angiography *Radiology* 95 (1970) 57
- and BOONSTEIN J J Differential problems in the angiographic diagnosis of carcinoma of the pancreas *Radiology* 96 (1970) 93
- REDMAN H C and JOSEPH R R Angiographic findings in pancreatitis *Amer J Roentgenol* 107 (1969) 46
- ROCHON J and BERT J Angiography of the pancreas *Amer J Roentgenol* 94 (1965) 182
- SURINOS B P NEAL M P ARISTAROV R H and HAGER H D Ten years experience with coeliac and upper abdominal superior mesenteric arteriography *Amer J Roentgenol* 101 (1967) 345
- SARLES H SARLES J C CAMATTE R MURATORE R GARIN M GUEN C PASTOR J and LEROY F Observations on 203 confirmed cases of acute pancreatitis: recurring pancreatitis and chronic pancreatitis *Gut* 6 (1965) 54
- STEELMAN R R DORLING R and CARTER R Surgical aspects of pancreatic abscess *Surg Gynec Obstet* 123 (1967) 75

- TYLEN U. Angiographic diagnosis of inflammatory disease of the pancreas. II. The differentiation from carcinoma of the pancreas. To be published in *Acta radiol. Diagnosis*.
- and DECKER H. Roentgenologic diagnosis of pancreatic abscess. *Acta radiol. Diagnosis* 14 (1973) 9.
- WARREN K. W., McDONALD W. M. and WEIDENHEIMER M. C. Trends in pancreatic surgery. *Surg. Clin. N. Amer.* 44 (1964) 743.

RADIOLOGIC PULMONARY FINDINGS IN HAEMOGLOBIN MALMÖ AND ERYTHROCYTOSIS

S BERGLUND and N M OHLSSO

The occurrence of erythrocytosis associated with the presence of an abnormal haemoglobin with increased affinity for oxygen Hb Malmo in several members of one family has been published (LORAN et coll 1970). A full clinical report of the family will be presented elsewhere by BERGLUND (1972). Several members also presented the same kind of pulmonary changes: these and Hb Malmo were thought to be caused by separate genes and the mode of inheritance of both was considered autosomal dominant. Two of the subjects who had the α changes as well as erythrocytosis died of microscopically identical anaplastic pulmonary carcinoma. The roentgen findings in family members with these pulmonary abnormalities are now reported.

Material The pedigree numbers used are the same as those in the clinical report. The material consisted of 7 family members with erythrocytosis and lung changes (see Table). Subjects III 20, III 22—23 and III 24 (the proband) were brothers and IV 19 the son of subject III 23. These 5 had erythrocytosis and almost identical roentgenographic findings in the chest. In all 5 with the

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Table

Data in 7 family members with erythrocytosis and idiopathic pulmonary fibrosis

Fno	Pedigree N	Sex	Age yrs	Hb g/100 ml	Radiologic findings in the chest		
					Nodular or reticular appearance	Vascular abnormalities	Carcinoma
	II 10	F	69	1			
			82	18.0	++	++	
4	III 20	M	58	21.0	+	+	
			68	19.7	++	++	
6-7	III 22	M	55	20.5	+	+	
			60	21.2	++	++	+
	III 23	M	51	17.1	+	+	
			62	18.2	++	++	
1-3, 5	III 24	M	45	1.8	+++	++	
			48	20.7	+++	++	+
	III 36	M	55	15.5	++	++	
	IV 19	M	21	18.4	+	-	

Hb = haemoglobin concentration; degree of pulmonary infiltrations: + = slight, ++ = moderate, +++ = marked; polycythaemia: + = marked.

exception of III 24 the presence of Hb Malmö was determined by electrofocusing in polyacrylamide gel or by oxygen binding investigations. These were not performed in subject III 24 as he died as early as 1963; he probably had Hb Malmö as no other cause for the erythrocytosis was evident. Subject II 10, maternal aunt of the 4 brothers without Hb Malmö, had developed polycythaemia vera with the same kind of lung changes. Her son, subject III 36, also had these changes but without Hb Malmö or other haematologic abnormalities.

Methods. Pa and lateral films of the chest were obtained in deep inspiration in all subjects. Angiography was carried out by means of a catheter introduced through a cubital vein into the pulmonary artery.

Results

The radiologic findings are summarized in the Table. Small nodular infiltrations, 1 to 2 mm in diameter, together with a reticular pattern gave the lungs a honeycomb appearance especially at the bases. The appearances were present in all 7 subjects to a varying degree but most marked in subject III 24; the pro-



Fig 1 Subject III 4 Chest P.A. Marked parenchymal interstitial and vascular changes typical of all subjects. Coarse reticular interstitial and small nodules with wide central pulmonary arteries but fine peripheral vessels.



Fig 2 Part of right lower lobe of subject III 24 (same film as in fig 1). Emphysematous blebs surrounded by coarse reticulum as well as fine peripheral arteries against the centrally dilated vessels.

postus) who had also apical bullous emphysema although merely slight in the youngest subject IV 19 who had only slight basal changes (Figs 1-2). Bronchography of the right lung in subject III 24 also disclosed well developed bronchiectasis of the lower lobe while the larger bronchi appeared to be normal.

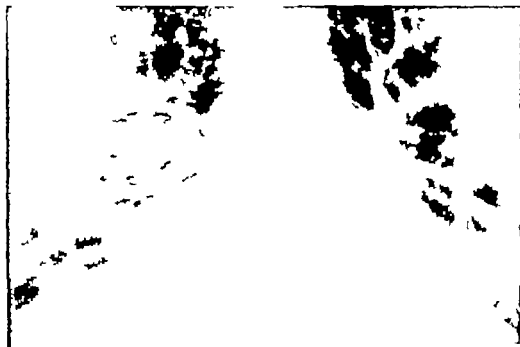


Fig. 3 Pulmonary angiography of subject III-4. a) Wide central pulmonary arteries against first generation branches. b) Enlarged part of posterj part of right lung.





Fig 4 Subject III 20 Angiograph. Evident changes in vessel diameter from central to second generation branches

The pulmonary vasculature was abnormal. The central arteries were dilated with abrupt tapering of the peripheral branches (Fig 1) in all 7 subjects except in the youngest IV 19. Angiography was performed in subjects III 20 and III 24 and revealed a characteristic pruned tree appearance with dilated central arteries and abrupt tapering of the arteries of the second generation (Figs 3-4). The arteries were also abnormal in that the calibre of long segments of the narrow peripheral arteries remained unchanged in contrast to the gradual tapering normally present. The peripheral vasculature was sparse and consisted of narrow arteries. Serial angiography indicated that the blood flow through the lungs was delayed.

Films obtained over a 10-year period in subjects III 20 and III 22-23 indicated some progression (see Table).

Subject III 24 developed peripheral rounded infiltrations of the right lower lobe due to anaplastic carcinoma (Fig 5). His brother subject III 22 later had a peripheral rounded infiltration of the left upper lobe and died of microscopically identical anaplastic carcinoma of the lung (Fig 6). It should be added that subject III 23 has in 1971 slight peripheral infiltration of the right upper lobe the nature of which has not been determined.



Fig. 5 Subject III 24. Wide spread and extensive reticular nodular and vascular changes. Multinodular anaplastic carcinoma appearing after 4 years of roentgenographic control.

Discussion

It is a remarkable coincidence that the two brothers III 22 and III 24 with erythrocytosis and the same type of roentgenographic changes developed microscopically identical pulmonary carcinoma. This sequence of events will be discussed in a separate report on the necropsy findings (BERGLUND & LARIL 1972).

The roentgenographic changes were strikingly similar in all 7 subjects examined. Autopsy in subjects III 22 and III 24 provided an opportunity to correlate the roentgen appearances with the pathologic findings. Pulmonary fibrosis in these 2 patients was conspicuous and was thought to correspond to the small nodular changes and reticular pattern observed in the roentgen examination. Subject III 24 had cystic bronchiectases up to a few mm in size as well as emphysema of the lung; these changes were less prominent in subject III 22. Both had dilatation of the central pulmonary arteries as well as hypertrophy of the right ventricle. The small arteries near the pleural surface were dilated and many contained thrombi. These small arteries were not identified with certainty in conventional films or at angiography. A lung section of subject III 22 prepared according to GOLON & WYERWORTH (1960) appears in Fig. 7.

Angiography presented the same pruned tree appearance as described in primary pulmonary hypertension by EVANS *et al.* (1957), HJELLBERG *et al.* (1959) and others. Subject III 24 and probably subject III 22 as well had



Fig 6 Subject III 22 Large solid tumour (anaplastic carcinoma) in left upper lobe appearing after 10 years of roentgenographic control typical reticular and nodular as well as vascular changes

pulmonary hypertension at rest Subject III 20 had normal pulmonary artery pressure at rest and in subject III 23 with dilated central pulmonary arteries the pulmonary artery pressure was normal both at rest and during exercise Thus wide central pulmonary arteries did not in these patients necessarily indicate the presence of pulmonary hypertension even during exercise

It is a well known fact that a large pulmonary artery may also be caused by increased blood flow but the cardiac output measured in subjects III 20 and III 23—24 proved to be normal

A pruned tree appearance has also been described in multiple peripheral pulmonary embolization (WILHELMSEN et coll 1963 WIENER et coll 1966) a condition in which pulmonary hypertension often occurs (WILHELMSEN et coll BJURK et coll 1967) No clinical signs of pulmonary embolization were observed however in the subjects examined Nevertheless the presence of thrombi in many small peripheral arteries was a striking feature in subjects III 22 and III 24 at necropsy and was probably related to the erythrocytosis These together with the pulmonary fibrosis may have been of some significance in the development of pulmonary hypertension in subject III 24 and pulmonary hypertension was probably also present in subject III 22 They may have been at least partly responsible for the probable delay in the blood flow through the lungs suggested in the serial pulmonary angiograms of subjects III 20 and III 24 the pulmonary vascular resistance was measured and proved to be slightly increased as would be expected with a reduced pulmonary capillary bed (BJURK et coll) It must

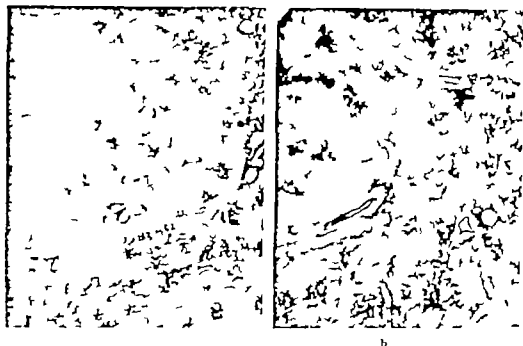


Fig. 1. (a) Part of normal lung. (b) The same part (of subject III 22) with water retention of the pleural surface and moderate tendency to honeycombing.

be emphasized, however, that the exact cause of the pulmonary hypertension evident in some of the subjects investigated is not known.

The appearance of the pulmonary vasculature in other patients with familial erythrocytosis would be of value for comparison with that in subjects with Hb Malmö. Films of the lungs of subjects with familial erythrocytosis including subjects with erythrocytosis caused by other abnormal Hb variant with increased affinity for oxygen have been reported as normal (MOUTAFFIAN *et coll.* 1967) reported the angiography as normal in a 20-year-old woman with familial erythrocytosis of unknown cause. Films of the chest of North American subjects with Hb Malmö have been described as normal (FAIRBANKS *et coll.* 1971) and have been examined by the present authors. A 40-year-old male had no parenchymatous or vascular changes as in Swedish subjects with Hb Malmö. Subject III 36 of the family now discussed had normal haematology but nevertheless pulmonary parenchymatous changes and abnormal vasculature. The relationship between these two pulmonary components is obscure and may well have to do with the hereditary character of the condition.

SUMMARY

Seven members of one family with haemoglobin Malmö an abnormal Hb associated with erythrocytosis proved to have the same type of roentgenographic changes in the lungs. These and Hb Malmö are thought to be caused by separate genes. Pulmonary fibrosis and an abnormal vascularity were the main findings at necropsy in two brothers of the family who died. Microscopically identical pulmonary carcinoma.

ZUSAMMENFASSUNG

Sieben Mitglieder einer Familie mit Hämoglobin Malmö einem abnormalen Hämoglobin verbunden mit einer Erythrozytose zeigten denselben Typus von röntgenologischen Veränderungen der Lunge. Es wird angenommen dass diese und Hämoglobin Malmö durch separate Gene hervorgerufen und Eine Lungenfibrose und eine abnormale Gefäßbildung waren die wesentlichen Befunde bei der Autopsie von zwei der Brüder dieser Familie die an mikroskopisch identischen Karzinomen der Lunge verstorben waren.

RÉSUMÉ

Sept membres d'une famille présentant une hémoglobine Malmö hémoglobine anormale associée avec une érythrocytose avaient le même type d'images radiographiques pulmonaires. Celles-ci et hémoglobine Malmö paraissent être causées par des gènes séparés. L'autopsie de deux frères de cette famille morts de cancers de poumon microscopiquement identiques a montré essentiellement une fibrose pulmonaire et une vascularisation anormale.

REFERENCES

- BERGELL, D. S. Erythrocytosis associated with haemoglobin Malmö accompanied by pulmonary changes occurring in the same family. *Scand. J. Haemat.* 9 (1972) 355.
- and LITTLE, F. Fibrosis and carcinoma of the lung in a family with haemoglobin Malmö. Anatomic findings. *Scand. J. Haemat.* 9 (1972) 424.
- BJÖRK, J., PALLER, S., SÖDERHOLM, B. and WIKMELSSON, L. Pulmonary gas exchange and hemodynamics in patients with recurrent pulmonary embolism and polycythemia vera. *Circ. et vasa* 9 (1967) 34.
- E. and W. SHOR, D. S. and BEDFORD, D. E. Solitary pulmonary hypertension. *Brit. Heart J.* 19 (1957) 9.
- FAIRBANKS, V. F., MALDONADO, J. E., CHARACHE, S. and BOYER, S. H. Familial erythrocytosis due to electrophoretically undetectable hemoglobin with impaired oxygen dissociation (hemoglobin Malmö $\alpha_2\beta_2$ #). *Proc. Mayo Clin.* 46 (1971) 721.
- GOLD, J. and WATSON, J. E. Thin sections of entire organs mounted on paper. In: Recent advances in pathology. Seventh edition, p. 80. Edited by C. A. Harrison, J. & A. Churchill Ltd. London 1960.
- KJELLBERG, S. R., MANKUTZ, E., REDDA, U. and JOHANSSON, B. Primary pulmonary hypertension. In: Diagnosis of congenital heart disease, p. 821. The Yearbook Medical Publishers Inc. Chicago 1959.

- LORAIN P. A., LEHMANN H., FAIRBANKS V. F., BERGLUND S. and LEONHARDT T. Two new pathological haemoglobins. Oligomeric beta 141 (H 19) Leu \rightarrow Arg and Malmo beta 97 (FG 4) His \rightarrow Gln. *Biochem. J.* 119 (1970) 68P.
- MOCTAFIAN J. J., GARRIZEL B., CARCASSONNE Y. et OLIVER J. Polyglobulie familiale à propos de deux cas. *Marseille méd.* 104 (1967) 107.
- WIENER S. N., EDELMAN J. and CHURCH B. L. Observations on pulmonary embolism and pulmonary angiogram. *Am. J. Roentgenol.* 98 (1966) 859.
- WILHELM L., SELANDER S., SÖDERHÖ M. B., PAULIN S., VARNVALL E. and WIKER L. R. current pulmonary embolism. *Medicine (Baltimore)* 42 (1963) 535.

RADIOGRAPHIC MEASUREMENT OF OVARIAN SIZE

M. LEA THOMAS R. TONGE and HELEN CARTY

Gynaecography is a well established method of demonstrating the female pelvic viscera, notably the uterus and ovaries. The method has been most extensively used to determine the size of ovaries in patients with hirsutism, oligomenorrhoea and infertility which constitute the Stein Leventhal syndrome (STEIN & LEVENTHAL 1935 STEIN 1964).

The most widely recommended measurement for the assessment of the ovarian size is the ovarian index which is a product of the maximum length and maximum breadth of an ovary (ABRAHAM'S & HUGHES 1955 BOWHAM *et coll* 1963 BUICE & GOULD 1957 EDWARDS & EVANS 1963 DAVIES *et coll* 1964 KENDALL 1967 LEA THOMAS *et coll* 1968 SCHULZ & ROSEN 1961 STEIN & LEVENTHAL 1935 STEIN 1964 STEVENS *et coll* 1966).

We have used statistical methods in an attempt to indicate which radiographic measurements of ovarian size are most likely to separate normal from enlarged ovaries.

Technique All the examinations were carried out by our standard technique (LEA THOMAS *et coll* 1968) except that instead of an artificial pneumothorax induction needle, we now use an 18 gauge 10 cm teflon catheter introduced

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- LORAIN P. A., LEHMANN H., FAIRBANKS V. F., BERGLUND S. and LEONHARDT T. T. o new pathological haemoglobins. Olmsted beta 141 (H 19) Leu → Arg and Malmo beta 97 (FG 4) His → Gln. *Biochem. J.* 119 (1970) 68P.
- MOUTAFFIAN J. J., GABRIEL B., CARCAMONNE Y. et OLMIER J. Polyglobule familiale à propos de deux cas. *Marseille méd.* 104 (1967) 107.
- WIENER S. N., EDELSTEIN J. and CHARNIS B. L. Observations on pulmonary embolism and pulmonary angiogram. *Arch. J. Roentgenol.* 98 (1966) 859.
- WILHELMSEN L., SELANDER S., SÖDERSTRÖM B., PAULIN S., VÄRBERG E. and WILKÖ L. R. current pulmonary embolism. *Medicine (Baltimore)* 42 (1963) 335.

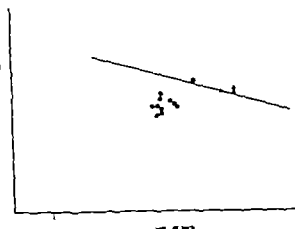


FIG. 1. Distribution of normal and polycystic patients around Z plotting average length against average width of both ovaries. Z = equation product of best discrimination. Δ = abnormal ovary. \circ = normal ovary.

C_1 and C are discriminate function coefficients and Z the equation product was expressed as a linear function of $C_1 X_1 + C X_2 + \dots + C_{10} X_{10}$.

The computer programme used calculated the value of Z for each pair of measurements for each individual patient.

Results

The equation products that is the points of best discrimination between the groups and the probability of correct allocation of a patient are shown in the Table.

From the table it can be seen that the most accurate allocation of a new patient into the normal sized or enlarged ovary group can be obtained by using the measurements average length and average width of both ovaries. For these measurements if Z falls above the equation product 0.28711 this patient has an 86% likelihood of having enlarged ovaries. The same principle can be applied to the use of the other measurements and the probability of correct allocation predicted.

Two pairs of the measurements are represented graphically in Figs 1 and 2. Fig. 1 shows the average length plotted against the average width of both ovaries in the abnormal and normal groups and Fig. 2 the distribution of the ovarian index of both ovaries in the groups. The line Z is the calculated best line of discrimination between the normal and abnormal patient.

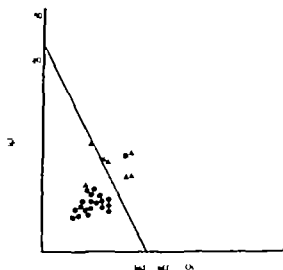


FIG. 2. Distribution of normal and polycystic patients around Z plotting the indices of both ovaries. Z = equation product of best discrimination. ▲ = abnormal ovary, ● = normal ovary.

Discussion

In our series all the abnormal patients had proven polycystic disease of the ovaries the commonest cause of ovarian enlargement. This however is not the only cause of enlargement and the possibility of ovarian cysts and tumours must be borne in mind when interpreting the films. Measurements alone cannot lead to a definitive diagnosis. This can only be reached by considering the films in conjunction with the clinical and biochemical data.

Nevertheless gynaecography is a well accepted and useful method of assessing ovarian size. It is particularly useful in demonstrating normal sized ovaries in patients with racial characteristics and infertility which may suggest the possibility of the Stein-Leventhal syndrome. The normal patients in our series all fell into this group and other causes of infertility were subsequently found.

Generally laparoscopy is now superseding gynaecography in the diagnosis of polycystic disease of the ovaries but this method is still not widely available throughout the world and gynaecography is a simple safe way of demonstrating the ovaries and is still extensively employed.

An ovarian index greater than 15 cm. is usually taken as indicating an enlarged ovary. Using this figure in patients with the Stein-Leventhal syndrome WEIGER & STEINBERG (1967) found that 30% of polycystic ovaries fell below this limit. Thus the application of the simple ovarian index to gynaecography gives an accuracy rate in separating patients with polycystic disease from normal patients in the region of 70%.

By using the indices of both ovaries in our formula we were able to improve the accuracy of predication to 82 %. However we recommend that the average length and average width of the ovaries be employed in the formula. Using these measurements and applying our formula to an individual patient if Z is greater than 0.28711 there is a probability of correct prediction of polycystic ovaries of 86 %. If Z is less than 0.28711 the probability of the ovaries being normal is 86 %. Thus we suggest is a worthwhile improvement on the more conventionally employed methods.

Although the formula $Z = C_1 \lambda_1 + C_2 \lambda_2$ appears complicated, in fact the answer can be obtained in a matter of seconds by the use of an electronic calculating machine now available in most hospitals.

Acknowledgement

We wish to record our thanks to Professor W. W. Holland and the Department of Clinical Epidemiology for conducting the statistical analyses.

SUMMARY

Various parameters of ovarian size on gynaecographic films were measured in two groups of 26 patients, one group having normal ovaries and the other polycystic disease. A formula has been devised which gives an accurate prediction of 86 % in separating normal from enlarged ovaries. It is suggested that the use of this formula represents a worthwhile improvement on the conventionally employed methods of assessing ovarian size by gynaecography.

ZUSAMMENFASSUNG

Verschiedene Parameter der Grösse des Ovars wurden an gynäkographischen Bildern bei zwei Gruppen von 26 Patienten gemessen, die eine Gruppe hatten normale Ovarien, die andere eine polyzystische Erkrankung. Es wurde eine Formel gefunden, die bei der Teilung normaler von vergrösserten Ovarien eine Genauigkeit der Vorhersage von 86 % gibt. Es wird empfohlen, dass der Gebrauch dieser Formel eine wertvolle Verbesserung der mehr konventionell angewendeten Methoden, die Grösse der Ovarien durch Gynäkographie zu bestimmen, darstellt.

RÉSUMÉ

Les auteurs ont mesuré différents paramètres des dimensions de l'ovaire sur des films d'gynécographie sur 2 groupes de 26 malades: un groupe ayant des ovaires normaux et l'autre une maladie polykystique. Ils ont mis au point une formule qui permet dans 86 % des cas de distinguer les ovaires normaux des ovaires augmentés de volume. Les auteurs pensent que l'usage de cette formule représente une amélioration notable par rapport aux méthodes utilisées habituellement pour déterminer les dimensions de l'ovaire par gynécographie.

REFERENCES

- ABRAHIM B. S. Pneumography as an aid to diagnosis of gynaecological disorders. *Amer J Obstet Gynec* 70 (1955) 1115.
- BONIFANT D. G., GROSSMAN M. E. and SIDAWAY M. F. Visualisation by gynaecography. *Clin Radiol* 14 (1963) 356.
- BURKE J. W. and GOULD D. M. Abdominal and pelvic pneumography. *Radiology* 69 (1957) 709.
- DANIELS M. L., DITLER W. C. and BRUNNER G. H. Pelvic pneumography. *Amer J Roentgenol* 92 (1964) 390.
- EDWARDS E. M. and EVANS K. T. Pelvic pneumography in Stein-Leventhal syndrome. *Brit J Radiol* 36 (1963) 46.
- HELDAL B. Pelvic pneumography. *Radiography* 33 (1967) 3.
- LEA THOMAS M., PRUNTY F. T. G. and SPATTON G. S. Gynaecography: primary amenorrhoea. *J Obstet Gynaec Brit Cwlth* 75 (1968) 625.
- RHODES P. The effects of wedge resection of the ovaries in 63 cases of Stein-Leventhal syndrome. *J Obstet Gynaec Brit Cwlth* 7 (1968) 1108.
- SCHULTZ E. and ROSEN S. W. Gynaecography: techniques and interpretation. *Am J Roentgenol* 86 (1961) 866.
- STEIN I. I. Duration of fertility following ovarian wedge resection—Stein-Leventhal syndrome. *West J Surg* 72 (1964) 237.
- , LEVENTHAL M. L. Amenorrhoea associated with bilateral polycystic ovaries. *Amer J Obstet Gynec* 29 (1935) 181.
- STEIN I. I., WEIGER J. F. and LEE R. S. Pelvic pneumography. *Med Radiol Technol* 4 (1966) 81.
- WEIGER J. F. and STEIN I. I. Pelvic pneumography in the diagnosis of polycystic ovaries including Stein-Leventhal syndrome. *Amer J Roentgenol* 100 (1968) 680.

ANGIOGRAPHIC DIFFERENTIATION BETWEEN INFLAMMATORY DISEASE AND CARCINOMA OF THE PANCREAS

U TYLEN

The angiographic criteria for the diagnosis of carcinoma of the pancreas are well established. Arterial encasement, sometimes complete occlusion, tumour vessels and venous compression or occlusion are the more common characteristics (LINDERQUIST 1965, BOOKSTEIN *et coll.* 1969, TAVERNER *et coll.* 1969, LECHNER *et coll.* 1970, OLSSON 1970, BOIJSEN 1971, BUCHHEIM *et coll.* 1971). The vascular changes in pancreatitis are also well known. The most prominent changes are smooth, regular stenosis of the arteries surrounding the pancreas and tortuous intrapancreatic arteries of slightly irregular lumen. Venous lesions are also frequent in this condition (HERNANDEZ *et coll.* 1967, REUTER *et coll.* 1969, BOIJSEN 1971, BUCHHEIM *et coll.* 1971, LECHNER & POKIESER 1971, TYLEN & ARANJÓ 1973).

In spite of the fact that the vascular changes in angiography in carcinoma of the pancreas and pancreatitis are considered characteristic, their angiographic differentiation may be difficult (ROSCH & BRET 1965, SAMMONS *et coll.* 1967, NEUBER & POLLARD 1967, MOSKOWITZ *et coll.* 1968, BOOKSTEIN *et coll.* 1969, FREDENS *et coll.* 1969, BOIJSEN 1970, LECHNER *et coll.* 1970, OLSSON 1970).

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1. BUCHHELER et coll 1971) This problem is accentuated by finding of inflammatory changes in the periphery of or distal (BILL 1971) This coexistence of the conditions makes it even at operation or biopsy (BIERSTADT 1959 GLENN & HALL 1965 MICAL 1965 LUND 1969)
2. the present investigation was to analyze the factors that in the light of the angiographic investigations in patients in whom the disease was evident and in whom a wrong diagnosis had been

Material and Methods A total of 87 patients with inflammatory disease of the pancreas examined by angiography during the 12 year period 1960 to 1971 has previously been analyzed and reported (TYLEN & ARNESEN 1973) The patients with carcinoma of the pancreas were examined during the same period. The diagnosis in the 87 patients was confirmed in every instance by operation or post mortem. The preoperative angiographic diagnosis was pancreatitis in 19 patients who later were proved to have carcinoma of the pancreas. Furthermore the angiographic diagnosis of carcinoma of the pancreas was made in 5 patients who were found at operation to have pancreatitis. The latter were followed for a minimum of two years postoperatively without evidence of malignancy. In addition 2 patients have been added, although the angiographic diagnosis was correct from the beginning since differential diagnostic problems were present. Thus 19 patients (13 men and 6 women) in whom differential diagnostic difficulties between malignant and inflammatory disease of the pancreas had occurred were selected. It should be pointed out that these 19 patients do not represent all those in whom an incorrect angiographic diagnosis had been made but only those in whom the particular problem had been to separate carcinoma of the pancreas from pancreatitis.

The angiograms were analyzed in retrospect according to the criteria of malignant and inflammatory diseases mentioned. The technical quality of the examinations was also evaluated to see how much this might have influenced the result.

Results

An analysis of the examinations was used to separate the patients into 7 groups. The groups were small but selected so that it might be possible to discuss patients in whom similar differential difficulties were present. Groups I to IV consisted of patients with confirmed carcinoma of the pancreas, groups V and VI those with pancreatitis and group VII those in whom the angiographic diagnosis in the long term was correct.



Fig. 1 Woman aged 55 with abdominal pain and loss of weight. Medial displacement of the gastroduodenal artery. Encasement of pancreatic arcades and tumour vessels in the head of pancreas. Alternate narrowings and dilatations in transverse pancreatic artery suggesting pancreatitis (→). Operation. Inoperable carcinoma.

I Missed diagnosis of carcinoma in spite of characteristic findings. This group comprised 4 patients in all of whom the diagnosis of carcinoma of the pancreas was made at the retrospective analysis. The diagnosis was based on encasement of arteries in all the patients and on tumour vessels as well in one patient. Two patients had only small branches of the pancreatic arcades or the dorsal pancreatic artery encased (Fig. 1) but in 2 patients encasement of large arteries such as the coeliac, superior mesenteric, common hepatic or splenic arteries was present. Venous lesions were demonstrated in 3 instances. The splenic vein was occluded in 2 patients and in one patient there was local constriction of the portal vein corresponding to the tumour site (Fig. 2). The lumen of the transverse pancreatic artery in one patient was slightly irregular as in inflammatory disease of the pancreas (Fig. 1). The technical quality of the examinations in the group was in 2 patients poor but regarded as sufficient in the other 2 patients.

II Incorrect diagnosis of pancreatitis due to poor technique. This group comprised 2 patients in whom changes suggestive of carcinoma of the pancreas were noted at the retrospective analysis. Due to poor technical quality of the examinations, however, the diagnosis could not be definitely established. In one of these patients who came for examination for probable gastric malignancy

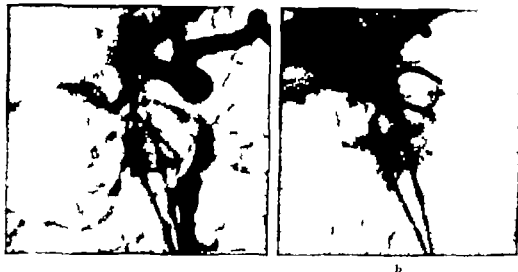


Fig. Man aged 63 with abdominal pain and jaundice. a) Medial displacement and stenosis of first parts of right hepatic and gastroduodenal arteries. b) Constriction of portal vein at corresponding artery (→). Operation: Inoperable carcinoma.

catheterization had been made only of the left gastric artery. The splenic artery was filled only by contrast medium that had spilled over. Nevertheless stenosis of the splenic artery was demonstrated and the splenic vein was also occluded (Fig. 3). The amount of contrast medium in the splenic artery did not permit evaluation of the character of the stenosis but the localized changes should have initiated extension of the examination to include injection of the coeliac artery.

In the other patient catheterization of the coeliac artery was repeatedly tried but at the injection of the contrast medium the catheter slipped out permitting only incomplete filling of the branches of the artery. In the splenic artery however changes were noted suggesting irregular encasement. The fine details were not possible to evaluate. Moreover at injection of the superior mesenteric artery it was noted that the intestinal branches were tortuous and irregular indicating involvement of the mesentery and the mesocolon.

III. Diagnosis of carcinoma established by repeat examinations. This group comprised 3 patients.

Case 1. Man aged 54 (Fig. 4) December 1968. Weight loss and jaundice. June 1969 operation at another hospital. Hard tumour with diameter of about 3 cm in head of pancreas. Choledochojunostomy. The patient was referred to our hospital March 1969 angiography. Slight changes in the gastroduodenal and pancreatic arteries suggestive of pancreatitis. Operation. Induration of the head of the pancreas. Necrosis in surrounding



b

Fig 3 Man aged 73 examined for possible malignant changes in stomach. a) I section of left gastric artery. Stenosis of first part of splenic artery. b) Occlusion of splenic vein at same location (→). Operation. Carcinoma of tail of pancreas.

tissues. Fine needle biopsy. No malignant cells. July 1970. Repeat angiography including superselective gastroduodenal injection to eliminate the last suggestion of carcinoma of the pancreas. Previous changes had disappeared. October 1970. Prolapse onising. Barium examination. Stenosis of the duodenum. Angiography. Encasement and occlusion of the pancreatic arcades - carcinoma of the pancreas. Operation. Carcinoma of the head of the pancreas. Total pancreatectomy.

No changes were evident at retrospective analysis making the diagnosis of malignancy possible at the first two examinations. The diagnosis was obvious at the third examination. The short interval between the last two examinations should be particularly noted.

Case. Man aged 60 (Fig 5). December 1965. Vague abdominal discomfort. Barium examination. Displacement of the duodenal loop. Angiograph. Stretched pancreatic arcades. Aneurysm in distal part of gastroduodenal artery. No operation. December 1966. Abdominal pain and jaundice. Exploration at another hospital. Tumour in the head of the pancreas regarded as carcinoma. Patient referred to our hospital. January 1968. Angiography. Irregular changes of the splenic artery probably due to pancreatitis. Malignancy could not be excluded. Operation and needle biopsy. Pancreatitis. Patient died in November 1968. Post mortem examination. Carcinoma of the pancreas with metastases in the liver.

No changes to suggest carcinoma of the pancreas were evident at retrospective analysis of the first examination. At the second examination the splenic artery was irregularly encased as was the transverse pancreatic artery. Occlusion of the splenic vein had also developed. The diagnosis of carcinoma of the pancreas should have been made. This angiographic diagnosis may have suggested further biopsies.



b



Fig. 4. C. 1 (guinea pig III). a) Testes normal. Seminiferous tubules of good diameter. Spermatogenesis proceeds slightly irregularly. b) One year later. Clusters have disappeared. c) Three months later. Seminiferous tubules of poor diameter. Interstitial glands (adenal) are displaced to the intertubular space. d) Adenoma.



FIG. Case (group III) a) First examination Displacement of pancreatic arcades due to enlargement of head of pancreas Aneurysm (→) in distal part of gastroduodenal artery b) Two years later Encasement of splenic and transverse pancreatic arteries Medial displacement of gastroduodenal artery Aneurysm as before

The third patient in this group was only examined once this demonstrated enlargement of the head of the pancreas with stretching of the pancreatic arcades and slight compression of the veins in the confluence The findings were verified at operation by needle biopsy In spite of the single angiographic examination the patient was placed in this group as he died a year and a half later of carcinoma of the pancreas The diagnosis was substantiated by cells compatible with this type of tumour in the ascites that developed during the terminal phase Retrospective analysis of the angiographic examination in this patient disclosed no changes consistent with carcinoma of the pancreas

IV *Incorrect diagnosis of pancreatitis due to presence of expansive lesions*
This group comprised 3 patients One of these had had several relapsing attacks of pancreatitis indicated by an elevation of the serum or urinary amylase The other two had been operated upon and the diagnosis of pancreatitis verified 9 and 12 years respectively before the angiographic examinations In one of these pancreatic calcifications were also demonstrated On the last admission the three patients all had abdominal pain and a palpable tumour in the epigastrium At angiography displacement of the gastroduodenal artery and the pancreatic arcades was noted as were lesions of the veins The diagnosis of expansive lesions probably pseudocysts of the pancreas was made At operation the expansive lesions in the head of the pancreas in 2 patients were highly differentiated adenocarcinomas with profuse production of mucus The tumours had thick highly vascularized walls and contained irregular cavities mucous filled In the third patient a pseudocyst distal to a carcinoma was evident

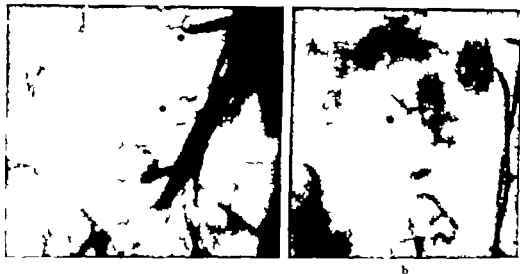


Fig. 6. Woman aged 66 with chronic calcifying pancreatitis for 9 years. Palpable mass in upper abdomen. a) Displacement of gastroduodenal artery and pancreatic vessels by expansive lesion in head of pancreas. Encasement of dorsal pancreatic artery. b) Widened branches of dorsal pancreatic artery (→) Irregular encasement. Operation: Highly differentiated adenocarcinoma.

Retrospective analysis revealed that the expansive lesions in the 2 patients with highly differentiated carcinomas had hypervascular walls. There was encasement of the small branches of the dorsal pancreatic artery and the pancreatic vessels respectively (Figs 6-7). In the third patient no changes compatible with the diagnosis of carcinoma of the pancreas were demonstrated. The technical quality of this examination was, however, not of the best.

Incorrect diagnosis of carcinoma due to localized vascular changes. This group comprised 4 patients with confirmed pancreatitis although the angiographic diagnosis was carcinoma of the pancreas. Three of these had similar conditions. There was a short history of abdominal pain and jaundice and at angiography irregular vessels in a small area of the head of the pancreas suggested the diagnosis of carcinoma (Fig. 8). One patient in addition had displacement of the pancreatic vessels due to enlargement of the head of the pancreas: a small localized tumour was evident at operation although biopsies from the tumour had disclosed pancreatitis, but no evidence of malignancy. One of the patients explored for a second time a few months later still had no evidence of malignancy. Another patient was subjected to repeat angiography two months later: the findings were similar with the exception that in addition changes evaluated as being postoperative had appeared.



Fig 7

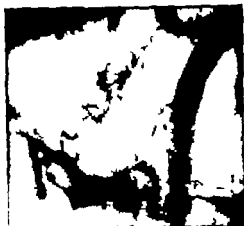


Fig 8

Fig 7 Man aged 38 with relapsing attacks of pancreatitis for several years. Jaundice and palpable mass in epigastrium. Displacement of gastroduodenal artery and pancreatic head by expansive lesion with low vascularization of center and hypervascularization of walls. Encasement of small arterial branches. Operation: Highly differentiated adenocarcinoma.

Fig 8 Man aged 50 with jaundice. Pancreatic arcades tortuous and irregular. Operation: Localized induration in head of pancreas. Biopsy: Pancreatitis.

The fourth patient in this group had cholecystectomy and choledochotomy for stones in the biliary tract. The pancreas was palpated and considered to be normal. Three months later the patient developed abdominal pain and loss of weight. Angiography demonstrated an expansive lesion in the head of the pancreas while stenotic changes of the gastroduodenal artery and irregular vessels in a small localized area suggested a malignant lesion (Fig 9). Operation revealed a pseudocyst but no neoplasm.

The retrospective analysis of the angiographic examinations in these 4 patients disclosed lesions that were irregular but not encased. Since they were strictly localized, however, any suggestion of malignancy could not be eliminated.

VI Missed diagnosis of pancreatitis in spite of characteristic findings. An erroneous diagnosis was made in one patient with a history of abdominal pain suggestive of chronic pancreatitis and reduction of the exocrine function of the pancreas. At angiography displacement to the left of the whole gland and the gastroduodenal artery was demonstrated and, in addition, branches of the dorsal pancreatic artery and the pancreatic arcades were slightly tortuous and irregular. The diagnosis of carcinoma of the pancreas could not be verified at operation; the whole of the pancreas was hard and indurated as in pancreatitis and malignancy was not evident at biopsy.

Retrospective analysis suggested pancreatitis from the extension of the vascular



Fig. 9. Male aged 67. Cholecystectomy 3 months before examination. Abdominal pain and loss of weight. Displacement and stenosis of gastroduodenal artery. Hypovascularization of head of pancreas. Localized irregular stenosis in superior pancreatic arcade (→) and its branches. Operation: Pseudocyst.

changes to the whole gland. The changes in the intrapancreatic vessels were of the type evident in inflammatory disease of the pancreas with alternating narrowing and dilatations, giving the vessels a beaded appearance.

VII. Correct angiographic diagnosis of carcinoma but with different diagnostic difficulties. The group comprised 2 patients.

Case 1. Woman aged 64. November 1963. Jaundice. January 1964 operation in another hospital. A hard pancreas with localized mass in the head, probably carcinoma. A biopsy. Cholecystoduodenostomy. April 1964. Jaundice. Operation. Changes less marked. Known. Increased pancreatic. Repeated attacks of jaundice followed. November 1964. Operation. The mass in the head of the pancreas had grown and a diagnosis of carcinoma was again made. Patient referred to our hospital. December 1964. Angiography. Encasement of the gastroduodenal artery and pancreatic arcades, tumour mass. Carcinoma of the pancreas. January 1965. Operation. The pancreas was hard and indurated with multiple small cysts of about 1 cm diameter. Biopsies. Fibrosis, no malignant cell. The patient died in May 1967. Autopsy. Huge carcinoma involving the whole pancreas.

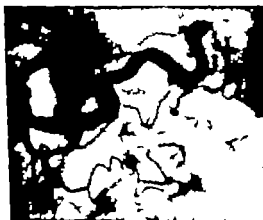
In retrospect there was no doubt regarding the angiographic diagnosis.

Case 2. Man aged 51 (Fig. 10). November 1965. Pneumonia on the left side. Flaccid urinary amyloid. Barium meal. Forward displacement of the stomach. Angiography. Irregular vessel in the tail of the pancreas with constriction of the splenic vein at the corresponding site. Probable malignancy. No operation. May 1966. Repeat angiography. The tumour changes had disappeared. March 1967. Pain and jaundice. April 1967. Angiography. Encasement of the splenic and coeliac arteries — carcinoma. Hepatic metastases. Operation. Inoperable carcinoma.

Retrospective analysis of the first examination suggested only small changes. The vessels, however, were more irregular than usually noted in pancreatitis. The constriction of the splenic vein at the same site pointed to the diagnosis of



b



d



Fig 10 Case 2 (group VII) a) b) First examination Arterial branches to tail of pancreas irregular and tortuous with constriction of splenic vein (\rightarrow) c) d) T months later Arteries unchanged constriction of splenic vein has disappeared e) One year later Irregular encasement of coeliac and splenic arteries Tumour mass (Courtesy of Butternorths)

carcinoma. At the next examination the venous changes had completely disappeared and could be explained by localized inflammatory swelling of the parenchyma surrounding and masking a small neoplasm. At the third examination the diagnosis was indisputable.

Discussion

No differential diagnostic difficulties usually arise in disease of the pancreas since the vascular changes in carcinoma and pancreatitis are characteristic. In spite of this, the patients in groups I and VI represent incorrect diagnosis although typical findings were demonstrated. This could have been avoided only by increased experience of angiography in pancreatic disease.

The second group of patients illustrates the importance of technical factors. In both patients in spite of the poor technique, vascular changes that permitted the diagnosis of pancreatic disease were demonstrated for different reasons: however the contrast filling of the pancreatic vessels was too sparse so that the diagnosis of carcinoma of the pancreas was not possible. Coming down of the roentgen beam, compression, superselective catheterization (ROSCIE 1969, REUTER 1969, TAJASHIMA *et coll.* 1970) and pharmacologic agents (BOIJSEN & RYDMAN 1967, CEM & ROSENBAUM 1969, UDÉN 1969, KAUDE & WILTANEN 1970) are possible means of improving the quality of the examinations.

The intestinal arteries in one of the patients in this group were tortuous and irregular suggesting malignant involvement of the mesentery. Similar changes are frequent also in pancreatitis, however (BOIJSEN & TYLEN 1972) and were therefore considered to support the diagnosis of pancreatitis. Whether or not differentiation between malignant and benign mesenteric involvement is possible must be further investigated but probably most of the changes in both conditions are due primarily to shrinkage of the tissues.

An interesting group is the third, comprising patients in whom in spite of good technical quality the diagnosis was not made at the first examination nor even in retrospect. The differential diagnostic difficulties are illustrated also by the fact that not even at operation and by needle biopsy was a carcinoma revealed. It is debatable whether malignancy is a complication of pancreatitis or if attack of pancreatitis are the first signs of a neoplasm of the pancreas (GAMMILL 1971). In one of the patients the diagnosis could be made in retrospect at the second examination and in another in whom three examinations were performed the diagnosis based on encasement of the arteries was made at the third. At this time the tumour was still resectable. This means that patients with inflammatory disease of the pancreas should have repeat angiography as soon as the character

of the disease alters so that malignancy may be revealed while radical surgery is still possible

The fourth group consisted of patients with expansive lesions of the pancreas previously diagnosed as pancreatitis. Pseudocysts usually arise as complications to inflammatory disease of the pancreas but it must be remembered that although infrequently they may occur in carcinoma (MIRAL 1965 HOWARD *et coll* 1967 BUCK & FLETCHER 1972). The expansive lesions in 2 of the present patients were however not pseudocysts with thin walls, but tumours with cystic degeneration the walls of the cysts being thick and highly vascular. This may permit differentiation if only the possibility of a malignant lesion be kept in mind. The differentiation of this type of cyst with thick walls from a hypervascular rim of compressed parenchyma sometimes occurring around pseudocysts of inflammatory origin may however be extremely difficult (HERNANDEZ *et coll* 1967 BORJES & TYLEN 1972).

Pancreatic calcifications were evident in one of the present patients (Fig. 6). Evidence of calcifications may further increase the bias in favour of a diagnosis of inflammatory disease of the pancreas. Calcifications in carcinoma of the pancreas seldom occur but a higher risk of malignancy in patients with calcifying chronic pancreatitis may exist (PAULINO-NETTO *et coll* 1960 LUNDH & NORDENSTAM 1970).

The vascular changes in pancreatitis are usually more extensive than those of carcinoma of the pancreas (BORJES 1970 REUTER *et coll* 1970). This should have pointed to the diagnosis in some of the patients in group I and II although knowledge of the same fact led to an incorrect diagnosis in the patients in group V. The localized changes in this group however were different from those in groups I and II in which they involved a large artery and a corresponding vein (Figs 2-3). In the former groups the vessels affected were small arterial branches which were irregular but not encased (Fig. 8). Occlusions were not evident. The differentiation in one of the patients was difficult even in comparison with tumour vessels (Fig. 9). This latter problem infrequently occurs although difficulties of differentiation may arise with average technical quality. Since the results of surgery in carcinoma of the pancreas are extremely poor (BRALL *et coll* 1970 FEDUSKA *et coll* 1971) every effort must be made to accelerate the diagnosis. On such terms an incorrect positive angiographic diagnosis based on localized vascular changes leading to exploratory laparotomy is perhaps the price to be paid if radical surgery is sometimes to be possible. Further refinement of the angiographic technique is one way to solve this problem of differentiation another is to repeat the angiographic examination within a short time as was done in the patients in group III.

The difficulties when inflammatory changes are coexistent with those due to

carcinoma. At the next examination the venous changes had completely disappeared and could be explained by localized inflammatory swelling of the parenchyma surrounding and masking a small neoplasm. At the third examination the diagnosis was indisputable.

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RÉSUMÉ

Les difficultés du diagnostic différentiel entre pancréatite et cancer du pancréas ont été étudiées sur 19 malades chez lesquels un diagnostic incorrect a été fait. Le diagnostic de cancer et particulièrement difficile en présence de lésions expansives et de calcifications. Un diagnostic fautive peut souvent être fait quand les lésions vasculaires étaient strictement localisées. Il est recommandé de répéter l'angiographie à de brefs intervalles quand il y a un doute. La qualité technique et l'expérience de l'angiographie pancréatique sont toutes deux extrêmement importantes.

REFERENCES

- BEALL S M, DYER G A and STEPHENSON H E. Disappointments in the management of patients with malignancy of pancreas. *Arch Surg* 101 (1970) 461.
- BORSTROM M. Surgical diagnosis of chronic pancreatitis and chronic relapsing pancreatitis. *Brit med J* 1 (1969) 938.
- BOTJEN E. Angiography in pancreatic disease. *Acta gastro-ent. belg* 33 (1970) 391.
— Pancreatic angiography. In: *Angiography*. Second Edition. Edited by H. L. Abrams. Little Brown and Company, Boston, Mass. 1971.
- and RUDMAN H C. Effect of epinephrine on celiac and superior mesenteric angiography. *Inver Radiol* 2 (1967) 184.
- and TRUB U. Vascular changes in chronic pancreatitis. *Acta radiol. Diagnosis* 12 (1972) 34.
- BOORTJEN J J, REUTER S R and MARTEL W. Angiographic evaluation of pancreatic carcinoma. *Radiology* 93 (1969) 757.
- BUCK B A and FLETCHER W S. Carcinoma associated with pancreatic cyst. *Surg. Gynec. Obstet* 134 (1972) 44.
- BUCHNER E, BOLDI I, FROMMELDT H and KAUFER C. Die angiographische Diagnostik der Pankreastumoren und der Pancreatitis. *Fortschr. Röntgenstr.* 115 (1971) 726.
- CAY M and ROSENBERG G. Zoliskographie mit Adrenalin. *Fortschr. Röntgenstr.* 111 (1969) 82.
- FEDORAK N J, DENT T L and LINDSAY S M. Results of palliative operations for carcinoma of the pancreas. *Arch Surg* 103 (1971) 330.
- FREEDMAN M, EGORIAN M and HART NATHAN F. The value of selective angiography in the diagnosis of tumours in pancreas and liver. *Radiology* 93 (1969) 764.
- GARNILL L E. Pancreatitis associated with pancreatic carcinoma: a study of 26 cases. *Proc. Mayo Clin* 46 (1971) 174.
- GLENN F and THORJANSSON B. Carcinoma of the pancreas. *Ann Surg* 159 (1964) 945.
- HERNANDEZ CL, ECARLAT B et BERNUTH V. L'arteriographie des affections pancréatiques. *J. Radiol.* 48 (1967) 327.
- HOWARD J M, TRAPNELL J R and PARENT F W. Distinction between pseudocysts of the head of the pancreas and carcinoma of the pancreas. *Ann Surg* 16 (1967) 293.
- KAUFER J V and WOLFAERT G W. Celiac epinephrine enhanced angiography. *Amer J Roentgenol* 110 (1970) 818.
- LEIBNER G and FORSTER H. Ergebnisse angiographischer Untersuchungen bei Pancreatitis. *Fortschr. Röntgenstr.* 14 (1971) 49.
— — ZAUENHAUER W und BRUNN P. Zur angiographischen Diagnose des Pankreaskarzinoms. *Fortschr. Röntgenstr.* 113 (1970) 340.

- LE D F. Carcinoma of the pancreas. Biopsy or not. *Acta chir scand* 135 (1969) 515
- LENDERQUIST A. Angiography in carcinoma of the pancreas. *Acta radiol* (196) Suppl No 735
- LUNDH G. and NORDENSTAM H. Pancreas calcification and pancreas cancer. *Acta chir scand* 136 (1970) 493
- MIRAL S. Operative criteria for diagnosis of cancer in a mass of the head of the pancreas. *Ann Surg* 161 (1965) 330
- MOSKOWITZ H. CHART A. and MELLINE H. Z. Tumour encasement of the coeliac axis due to chronic pancreatitis. *Amer J Roentgenol* 104 (1968) 641
- NEBASUR R. A. and POLLARD J. J. A critical evaluation of selective coeliac and superior mesenteric angiography in the diagnosis of pancreatic disease particularly malignant tumor facts and artefacts. *Radiology* 89 (1967) 1017
- OLSON O. Angiography in tumours of the pancreas. In: *Modern trends in diagnostic radiology*. Edited by J. W. McLaren. Butterworths London 1970
- PALLINO NETTO A. DREILING D. A. and BARONOWSKY I. D. The relationship between pancreatic calcification and cancer of the pancreas. *Ann Surg* 151 (1960) 530
- REUTER S. R. Superselective pancreatic angiography. *Radiology* 92 (1969) 74
- REDMAN H. C. and JOSEPH R. R. Angiographic findings in pancreatitis. *Amer J Roentgenol* 107 (1969) 56
- — and BOOKSTEIN J. J. Differential problems in the angiographic diagnosis of carcinoma of the pancreas. *Radiology* 96 (1970) 93
- ROSCIT J. Superselective arteriography in the diagnosis of abdominal pathology. Technical considerations. *Radiology* 92 (1969) 1008
- and BRET J. Angiography of the pancreas. *Amer J Roentgenol* 94 (1965) 18
- SAMMONS B. P. NEAL M. P. ARMSTRONG R. H. and HAZEN H. D. Ten years experience with coeliac and upper abdominal superior mesenteric arteriography. *Amer J Roentgenol* 101 (1967) 345
- TAKASHIMA T. YAMAMOTO I. MITANI I. and SUTO M. Transfemoral superselective coeliac angiography. *Amer J Roentgenol* 110 (1970) 813
- TAVERNIER J. DELORME G. LAFITTE J. TESSIER J. et BELLET M. Apports de l'angiographie coelique et mésentérique à la radiographie pancréatique. *J Radiol* 50 (1965) 167
- TYLEA L. and ARIMOTO B. Angiographic diagnosis of inflammatory disease of the pancreas. *Acta radiol* Diagnosis 14 (1973) 215
- ULLEN R. Effect of secretin in coeliac and superior mesenteric angiography. *Acta radiol* Diagnost 8 (1969) 497

ALTERATIONS IN PYLORO DUODENAL JUNCTION FOLLOWING VAGOTOMY AND PYLOROPLASTY

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Vagotomy with a drainage procedure has become a recognised method in the treatment of duodenal ulcer during the last 20 years. LA COUR ANDERSEN *et coll* (1971) recently reviewed the results in 190 patients subjected to total vagotomy and pyloroplasty (*ad modum* Weinberg) as an elective operation in the treatment of duodenal ulceration. Their work included a review of the possible drainage methods as well as the relevant literature. Most reports concern themselves largely with operative techniques and clinical results; few afford information on the roentgenologic appearances at the pyloro-duodenal junction after pyloroplasty.

The present research was specifically focussed upon the alterations in a series of 67 patients subjected to vagotomy and pyloroplasty *ad modum* Weinberg. TOYE *et coll* (1970) have described the alterations after Heimke—Mikulicz pyloroplasty and SOLANKE & KOLAWOLE (1971) and PEDERSEN (1971) have reported similar alterations after Weinberg pyloroplasty. The appearances expected included constrictions in the antrum and first part of the duodenum, an impression in the lumen at the site of the suture line overlying the severed pylorus.

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- LUND F. Carcinoma of the pancreas. Biopsy or not? *Acta chirurgica* 135 (1969) 515
- LUNDEQUIST A. Angiography in carcinoma of the pancreas. *Acta radiol* (1965) Suppl No 235
- LUNDH G and NORDENSTAM H. Pancreas calcification and pancreas cancer. *Acta chirurgica* 136 (1970) 493
- MIRAL S. Operative criteria for diagnosis of cancer in a mass of the head of the pancreas. *Ann Surg* 161 (1965) 595
- MORROWITZ H, CHAIT A and MELLING H Z. Tumour encasement of the coeliac axis due to chronic pancreatitis. *Amer J Roentgenol* 104 (1968) 641
- NEBESAR R A and POLLARD J J. A critical evaluation of selective celiac and superior mesenteric angiography in the diagnosis of pancreatic disease particularly malignant tumor facts and refacts. *Radiology* 89 (1967) 1017
- OLSSON O. Angiography in tumours of the pancreas. In: *Modern trends in diagnostic radiology*. Edited by J W McLaren. Butterworths London 1970
- PAULINO NETTO A, DREILING D A and BAROWITZ I D. The relationship between pancreatic calcification and cancer of the pancreas. *Ann Surg* 151 (1960) 530
- REUTER S R. Superselective pancreatic angiography. *Radiology* 92 (1969) 74
- REDMAN H C and JOSEPH R R. Angiographic findings in pancreatitis. *Amer J Roentgenol* 107 (1969) 56
- and BOONSTEEN J J. Differential problems in the angiographic diagnosis of carcinoma of the pancreas. *Radiology* 96 (1970) 93
- ROSEN J. Superselective arteriography in the diagnosis of abdominal pathology. Technical considerations. *Radiology* 92 (1969) 1008
- and BRIST J. Angiography of the pancreas. *Amer J Roentgenol* 94 (1965) 182
- SAMMONS B P, NEAL M P, ARMSTRONG R H and HAGER H D. Ten years experience with celiac and upper abdominal superior mesenteric arteriography. *Amer J Roentgenol* 101 (1967) 345
- TAKAHISHI T, YAMAMOTO I, MITANI I and SHIY M. Transfemoral superselective celiac angiography. *Amer J Roentgenol* 110 (1970) 815
- TAVERNIER J, DELORME G, LAFITTE J, TESSIER J et BELLET M. Apports de l'angiographie coeliaque et mésentérique à la radiographie pancréatique. *J Radiol* 50 (1969) 867
- TYLÉN U and ARONSSON B. Angiographic diagnosis of inflammatory disease of the pancreas. *Acta radiol* 14(1973) 215
- UNIK R. Effect of secretin in celiac and superior mesenteric angiography. *Acta radiol* 8 (1969) 497

Table 1

Röntgen findings before and six months after operation

	Niche		Deformity	
	+	-	+	-
Before operation	55	10	65	2
Two months after operation	30	35	59	6

Table 2

The differentiated occurrence of retention before and after operation

Before operation	Six months after operation		
	No retention	Retention grade I	Retention grade II
54 no retention	40	13	1
10 ret. grade I	2	6	2
1 ret. grade II	0	0	1

of the 65 patients remaining was 15 men and 3 women under 40 years, 28 men and 5 women between 40 and 60 years and 12 men and 2 women over 60 years.

A standardized radiologic technique included the administration of 100 ml of barium and special views of the duodenal bulb. Gastric emptying rates were estimated from 4-hour films. The authors examined the films with no foreknowledge of the results of earlier examinations or of the operation findings. Attention was concentrated on the criteria of niche deformity and retention. Retention was classified as no retention, retention grade I without dilatation and with normal mucosal relief, and retention grade II with dilatation (Tables 1, 2).

Results

Ulceration was demonstrated before operation in 55 patients while in a further 8 some deformation of the bulb was evident. Two patients came to operation in the absence of any evidence of ulceration; an ulcer was present in one of these and the other had a typical history with a raised peak acid output of 65 mEq/h but no ulcer.

The postoperative roentgen examination was apparently normal in 6 patients with no evidence of ulcer or pyloroplasty. No less than 30 of the 65 patients

were considered to have ulceration. Table 2 gives the retention figures as reflected by the 4 hpc films. Before operation 54 patients had no retention, 10 had retention grade I and one retention grade II.

Following operation 13 patients (24 per cent) without retention had developed grade I retention and one grade II retention. Retention was relieved in 2 of the 10 grade I patients, while in 2 others the retention had progressed to grade II. The only pre-operative grade II patient failed to improve by operation.

One effect of the operation was thus increased delay in the gastric emptying.

Seven of the 65 patients (11 per cent) had positive insulin tests as judged from the Hollander criteria — 4 early and 3 late. No relationship was apparent between the roentgenologic and insulin test results.

Discussion

Familiarity with the post-pyloroplasty appearances of the pylorus region is essential in the roentgenologic assessment of patients with possible recurrent ulceration (WILLIAMS & TOYE 1970; FREDENS *et coll.* 1971). The difficulties are emphasized by the fact that 30 patients of the present material were reported as still having ulceration after operation. None of these patients was operated on for recurrence and confirmation of the findings is lacking. The proportion of wrong reports thus remains unknown.

Gastric emptying was clearly retarded after the vagotomy and Weinberg pyloroplasty. This observation has also been made previously (BROOKS 1970), but in general is at variance with the usual reports of gastro-intestinal hurry and diarrhoea.

The clinical significance of retention is apparently not marked. None of the 19 patients with grade I retention at control had any symptoms and operation was not considered in the 4 patients with grade II retention. It is not worthy that these 4 patients no longer had retention when investigated between six months and two years later. The series, however, involved patient selection because all those with severe pyloric or duodenal changes underwent primary resection or gastroenteroanastomosis.

SUMMARY

Sixty-five patients with duodenal ulceration were treated by total abdominal vagotomy and Weinberg pyloroplasty. Gastric retention increased after the operation but seemed not to be of clinical significance in this selected group of patients. Knowledge of the postoperative changes in the roentgenologic appearances to be expected after various forms of pyloroplasty is essential for the postoperative evaluation, especially when a possibility of recurrent ulcer

ZUSAMMENFASSUNG

Fünfundsechzig Patienten mit Duodenalulcus wurden durch total abdominale V-gotomie und Pyloroplastik nach Weinberg behandelt. Die Retention des Magens zuzug nach der Operation schien jedoch in dieser selektierten Patientengruppe ohne klinische Bedeutung zu sein. Kenntnisse der besonderen Veränderungen im roentgenologischen Bild die nach verschiedenen Formen von Pyloroplastik erwartet werden können sind für die postoperative Beurteilung wesentlich, besonders wenn die Möglichkeit eines Rezidivs obliegt.

RÉSUMÉ

Soixante-cinq malades atteints d'ulcère duodénal ont été traités par vagotomie abdominale totale et par pyloroplastie de Weinberg. La rétention gastrique a été augmentée après l'opération mais ne paraît pas avoir d'importance clinique dans ce groupe sélectionné de malades. Il est essentiel de connaître les modifications particulières d'aspect radiologique auxquelles on peut s'attendre après les différentes formes de pyloroplastie de façon à faire un bilan postopératoire en particulier quand il existe une possibilité de récurrence.

REFERENCES

- BROOKS F P. Digestive disease. *Amer J dig Dis* 15 (1970) 1039.
FRIEDMAN M, KRONBERG O, MADSEN P and PALMBERG J. Gastrointestinal hormones and other subjects. In: *The Fifth Scandinavian Conference on Gastroenterology*. Ålborg, Denmark 1971. Munksgaard, Copenhagen 1971.
LA COUR ANDERSEN J, CLAUSEN B og MØLLER HANSEN M. Ulcus duodeni og pyloroplastik total vagotomi — en Weinberg som selektiv operation på 190 ptt med ulcus duodeni. (In Danish.) *Ugeskr Læg* 133 (1971) 975.
PEDERSEN G. Hypoton duodenografi. (In Danish.) *Nord Med* 16 (1971) 1081.
SOLANKI T F and HOLAWOLE T M. The evaluation of vagotomy and pyloroplasty in the treatment of duodenal ulcer in Nigerians. Clinical and radiological study. *Brit J Surg* 58 (1971) 193.
TOYE D K, M HUTTON J F K and WILLIAMS J A. Radiological anatomy after pyloroplasty. *Gut* 11 (1970) 358.
WILLIAMS J A and TOYE D K M. Recurrent ulcer after vagotomy and pyloroplasty: the X-ray appearances and their value in diagnosis. *Gut* 11 (1970) 40.

CONTRACTION OF THE BORDER OF THE ISCHAEMIC LEFT VENTRICLE IN DOGS

N E AHLBERG and T SEZMAN

The introduction of electrokymography by HENRY & BOONE (1945) was followed by great expectations that it would afford information about the movements of the heart. The method has also been used for the diagnosis of diseases of the heart valves (RUDHE 1956 BARTLEY 1960) and its application in coronary arterial disease has been considered. It has been claimed that the method demonstrates pathologic wall movement in myocardial infarction both from the ventricular border (LUISADA & FLEISCHNER 1948 GILLICK & REYNOLDS 1949 SCHWEDEL *et coll* 1950 DACK *et coll* 1950 DACK 1955 BARTLEY 1960) and the left atrium (BARTLEY 1955). In addition, prolongation of the phase of isovolumetric relaxation has been demonstrated by electrokymography in patients with myocardial infarction (BARTLEY 1960).

The impaired contractility of myocardial muscle following acute ischaemia (TENNANT & WIGGERS 1935 FROMEL & PIRA 1957 TATOOLES & RANDALL 1961) causes changes in both the shape and movement of the ventricle. A cine angiographic technique (AHLBERG *et coll* 1972) has previously indicated that the normal increase in wall thickness during systole fails to appear as the ventricle remains somewhat dilated. The movement of the ventricular border on the other hand seems to be only moderately affected. Objections may be raised however that the cineangiographic method is limited in its ability to evaluate

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the movement of the outer border of the ventricle. It was therefore considered that it might be of interest to investigate the movement of the border by electrokymography after experimentally induced myocardial ischaemia in dogs.

Material and Methods The investigation was performed in 15 mongrel dogs (15 to 25 kg) anaesthetized with pentobarbital curarized and ventilated with a N₂O—O₂ mixture in an Engstrom Respirator. The heart was exposed by left sided thoracotomy and a short section of one or two central branches of the left anterior descending coronary artery were dissected for subsequent occlusion. This was done with snares at levels that were expected to produce ischaemic areas of up to 30 per cent of the left ventricle. Metal indicators were sutured to the epicardium within the ischaemic areas facilitating proper identification and positioning of these areas in the roentgen television system. The pericardium was then closed and the snares drawn out through the chest wall. The thorax was closed and extubated.

The electrokymograms were recorded immediately after the operation. The animals were placed on the left side, slightly tilted so that the area of the left ventricle marked by the metal indicator was depicted tangentially. The phototubes of the electrokymograph (Elema Schonander type RCA 1 P 121) had a slit of 16 mm × 6 mm the roentgen tube being energized by 50 c/s A.C. and placed under the table. Kymographic disturbances caused by variations in the mains voltage were reduced to a minimum by subtracting the current of an additional photocell on the roentgen tube from that of the pick up photocell above the animal. The kymographic signal was filtered so that all frequencies above 40 c/s were eliminated so that the least possible time lag was 0.01 s. The kymographic recordings were registered on an optical electrocardiograph (Elema Klinik) simultaneously with the electrocardiogram, phonocardiogram and pressure tracings from the ascending aorta, left ventricle and left atrium. The electrokymographic recordings were made before, during and after the coronary artery occlusions with constant positions of the animal and the recording equipment. The receptor slit of the phototube was placed perpendicular to the indicated region of the left ventricular surface so that the contour examined always moved in the central part of the slit. The recordings were made before the coronary occlusion and repeated 1, 2, 4 and 6 minutes after occlusion. The occlusion was then released and in some series new recordings were made during the first ten minutes of recovery. In one animal electrokymograms were also recorded from the dorsal non ischaemic border of the left ventricle before and during occlusion. The effectiveness of the arterial occlusions was controlled by ECG and in some experiments by selective coronary angiography.

Cineangiographic recordings of the left ventricle were obtained immediately

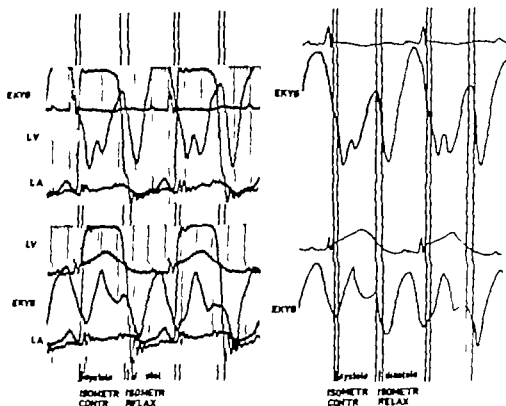


Fig. 1. Electrocardiograms from the entral border of the left ventricle corresponding to the ischaemic area recorded simultaneously with electrocardiogram and pressure tracings from the left ventricle (LV) and the left atrium (LA) before (a top) and during (b bottom) ligation of the left anterior descending coronary artery.

before the electrocardiograms in 4 animals. The left ventricular volume were calculated from the cineangiographic frames corresponding to end diastole and end systole by a method previously described (AHLBERG *et al.* 1978).

The ischaemic region of the left ventricular wall was removed at the end of the experiments and calculated as a percentage of the total left ventricular weight.

Results

The entire investigation consisted of 31 experiments in 15 dogs. Fifteen experiments were excluded since the occlusions could not be confirmed by changes in the ECG or by selective coronary angiography. The results thus represent 17 experiments in 9 dogs. Figs 1 to 4 are electrocardiograms obtained

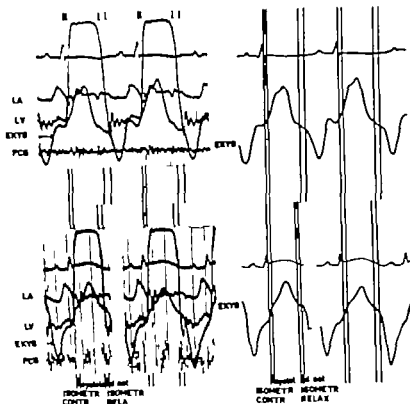


Fig. 4. Electrophysiological tracings from the central border of the left ventricle recorded simultaneously with electrocardiogram, phonocardiogram (PCG) and pressure tracings from the left ventricle (LV) and the left atrium (LA) before (a) and during (b) occlusion of the left anterior descending coronary artery.

from four different parts of the left ventricular border in 3 different animals. Before occlusion the electrophysiological curves presented marked variations in direction and amplitude of the movements obtained from different parts of the ventricular border of the ventricle. Electrophysiological tracings with typical monophasic inward movements during systole and outward movements during diastole were obtained only in a few experiments (Fig. 4 a) and were recorded from different parts of the ventricular border. The electrophysiological tracings in most experiments had biphasic appearances both in systole and diastole (Figs 1 a and 2 a). The main direction of movement during systole was inwards in 10 and outwards in the remaining 7 experiments. Before occlusion of the coronary artery the electrophysiological tracings displayed large variations in amplitude and directions both in the isovolumetric contraction and isovolumetric relaxation phases.

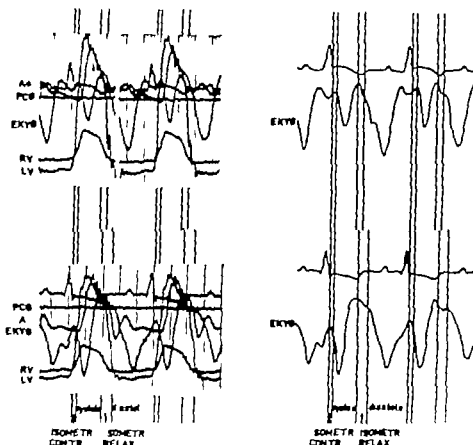


Fig. 3. Electrophysiological tracings from the ventral border of the left ventricle recorded simultaneously: (a) with electrocardiogram, phonocardiogram (PCG) and pressure tracings from the ascending aorta (Ao), the left ventricle (LV) and the right ventricle (RV) before (top) and during (bottom) occlusion of the left anterior descending coronary artery.

The electrocardiograms obtained from the part of the ventral border corresponding to the ischaemic region during myocardial ischaemia indicated changes opposite to those of the curves obtained from the dorsal non ischaemic wall. These changes in the ischaemic region had no particular features although there was a general diminution in the inward movement or an increase of the outward movement during systole (Figs 1 b, 2 b, 3 b, 4 b). The electrocardiographic changes in most experiments were moderate but in one there were marked changes in the shape of the electrocardiograms, especially in the early part of systole with abolition or reversal of the inward movement (Fig. 1). The changes in the movement in diastole during coronary artery occlusion were generally limited to its diminution outwards (Fig. 3).

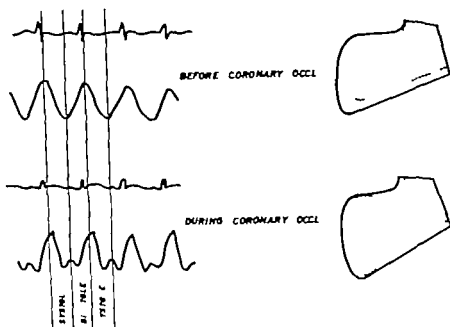


Fig 4 Drawings of electrokymograms from the entral border of the left ventricle corresponding to the ischaemic area and left ventricular cavity from cineangograms in end diastole (—) and end systole (---) recorded in direct succession before (top) and during (bottom) occlusion of the left anterior descending coronary artery

The electrokymographic changes during myocardial ischaemia usually appeared as early as one to three minutes after the occlusion and remained constant

The electrokymograms from half of the experiments partly returned to normal within the first ten minutes after release of the coronary artery occlusion

Obvious difficulties existed in quantitating the changes in amplitude in the electrokymograms and therefore in correlating these to physiologic parameters. No correlation between the electrokymographic changes and the size of the ischaemic region or the alteration in the volume of the left ventricular cavity was evident (see Table). The appearances of the ventricular cavity changed during systole to a club or pear shape immediately after the coronary artery occlusion (Fig 4). The cavity was only slightly dilated during diastole without any changes in the shape. The left ventricular volumes in end systole increased from 28.5 ml (SE 2.2) before to 42.7 ml (SE 3.1) after occlusion and the volumes in end diastole from 55.4 ml (SE 5.7) to 62.3 ml (SE 4.7). The increase in end systolic volume was significantly correlated to the size of ischaemic area ($p < 0.05$).

Table

Correlation between size of ischaemic region, electrokymographic changes and changes in volume of the left ventricular cavity

Ischaemic region as percentage of left ventricular weight	Qualitative changes of electrokymograms	Main direction of the electrokymograms during systole before coronary artery occlusion	Increase in end systolic volume during coronary artery occlusion as percentage of value before occlusion	Increase in end diastolic volume during coronary artery occlusion as percentage of value before occlusion
27	++	Inward	+	-
30	+	Inward	82	10
30	+	Outward	62	3
30	+	Outward	46	30
13	+	Inward	31	18
19	+	Inward	37	8
25	++	Inward		
25	++	Inward		
25	++	Inward		
25	+	Inward		
22	++	Inward		
22	0	Inward (non ischaemic area)		
29	++	Outward		
22	+	Outward		
22	+	Outward		
22	++	Inward		
31	+	Outward		

Changes in the movement of the left ventricular border have thus been demonstrated with electrokymography in all dogs during coronary occlusion. A discrepancy however existed between the prominent changes in configuration of the left ventricular cavity and the relatively small changes in the electrokymograms obtained from the border of the ischaemic area of the left ventricle.

Discussion

Electrokymography enables the movements of the ventricular border to be registered and analyzed since the tracings instantly reflect these movements. Changes in illumination of the receptor screen are due to variations in roentgen absorption which depend mainly on the movements of the heart border examined. The electrokymographic curves register the border movements with precision.

mon both in time and direction. The amplitude, however, is not linearly reflected in the electrokymogram (ZINSSER *et coll* 1950) so that the border movements are more or less distorted.

This may be one reason why the configuration of the tracings obtained from the ventral border of the left ventricle varies considerably in the normal state. Another explanation for this may be that the movement of the border should be regarded as a composite effect of the outward and inward movements of the ventricular wall and pendulating and rotating movements of the heart. Only during ideal conditions when these inward and outward movements of the wall dominate, do the border movements in the electrokymogram resemble a ventricular volume curve (DACK 1950). Preponderance of the other two heart movements, however, may influence the composite effect in such a way that the tracing will have a shape very different from that of a volume curve. The border movements may therefore be mainly inwards, outwards or biphasic in both systole and diastole depending on the movement or movements that dominate the region of the border recorded. The different directions of movement during isovolumetric contraction and relaxation may be explained in the same way.

The deterioration in myocardial contractility that rapidly follows acute coronary artery occlusion (TENNANT & WIGGERS 1935) changes the shape and movement of the left ventricle (AHLBERG *et coll* 1972) and it is remarkable that the ventricular cavity changes more than the ventricular contour. Moreover registration with electrokymography in the present investigation revealed only moderate changes in movement and there was no evidence of paradoxical movements of the border of the ischaemic area of the ventricle. This is also supported by the fact that the radiologic examination of a heart usually fails to demonstrate any localized bulge of the left ventricular border during the acute phase of myocardial infarction.

The changes in movement during acute myocardial ischaemia registered with electrokymography in the present investigation are in agreement with some of those recorded in patients with myocardial infarction (DACK 1950; BARTLEY 1960). As opposed to the present findings, however, partially and completely paradoxical movements of the ventricular border have been demonstrated in the patients, these suggesting that the ischaemic part of the myocardial wall acts dynamically as a ventricular aneurysm (GILLICK & REYNOLDS 1949; SCHWABEL *et coll* 1950; DACK *et coll* 1950; TUMANOWSKI *et coll* 1961). These recordings were, however, generally made one or more weeks following coronary artery occlusion. The present investigation supports the assumption that the ischaemic wall does not bulge immediately after coronary artery occlusion while quite a different situation exists in the late stages of myocardial damage. If the ischaemic region be large enough collateral blood flow will not suffice to prevent total

muscle necrosis with the risk of development of an aneurysm and resulting in the border movements quite different from those evident in the acute stage.

The large variation in the electrokymographic changes without signs typical of myocardial rechaemia may be explained by the alterations in the pendulating and rotating movements of the heart, which may influence the border movement of the ischaemic ventricular area in different ways. Another explanation for these variations may be that the electrokymograms recorded from the ventral border of the left ventricle may be influenced by movements of the right ventricle. The lateral border of the left ventricle might thus be a more suitable region. However the ventral border was chosen because the experimental technique was based on occlusions of the left anterior descending coronary artery. Furthermore, the area to be investigated was revealed by a metal indicator which means that the same spot of the ventricular border was examined before, during, and after coronary occlusion. It is therefore unlikely that the movements of the right ventricle could influence the findings.

A previous investigation indicated that rechaemia is followed by impaired muscle function with changes in shape and movement of the left ventricle within two minutes following coronary artery occlusion (AHLBERG *et al.* 1972). It was demonstrated that even thirty minutes after release of the ten minute occlusion slight residual changes in the ventricular cavity were evident. This was confirmed by the present investigation of border movements. The change in the electrokymograms appeared within one to three minutes of occlusion and remained to some extent after its release, this was in spite of the fact that the changes in ECG disappeared rapidly and the selective coronary angiogram disclosed a completely patent vessel lumen immediately after release of the occlusion. This means that impaired muscle function due to acute ischaemia is also reflected in the movements of the ventricular border.

The ventricular border corresponding to the ischaemic region presented moderate changes during acute coronary artery occlusion. This was demonstrated by electrokymography in the present investigation and previously by cineangiography. The changes in the electrokymographic curve were always demonstrated although they varied considerably in shape and magnitude and were therefore difficult to quantitate and correlate to physiologic parameters. The electrokymographic method thus seems to be limited in its ability to diagnose acute ischaemic changes in the wall of the left ventricle.

Acknowledgement

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SUMMARY

An electrokymographic investigation of the ventral border of the left ventricle was performed in dogs. The changes in the electrokymographic curves during occlusion of the left anterior descending coronary artery were analyzed and compared to those in the left ventricular cavity examined with simultaneous cineangiography.

ZUSAMMENFASSUNG

Eine elektrokymographische Untersuchung der ventralen Kante des linken Ventrikels wurde an Hunden vorgenommen. Die Änderungen der elektrokymographischen Kurven während des Verschlusses der Arteria coronaria descendens anterior wurden analysiert und mit den Veränderungen der Kavität des linken Ventrikels, erlitten die gleichzeitige angiokymographisch untersucht worden waren.

RÉSUMÉ

Les auteurs ont fait une étude électrokymographique du bord antérieur du ventricule gauche sur des chiens. Ils ont examiné les modifications des courbes électrokymographiques pendant l'occlusion de l'artere coronaire descendante antérieure gauche et les ont comparées celles de la cavité ventriculaire gauche examinées par angiographie simultanée.

REFERENCES

- ANDERSSON N. E., PALLIN S. and SIEGMAN T. Left ventricular changes during coronary artery occlusion in dogs. *Acta radiol. Diagnosis* 12 (1972) 789.
- FRIENLMO L., LINDHOLM M. and SIEGMAN T. Cineangiographic estimation of the left ventricular volume during acute myocardial ischaemia in dogs. *Acta radiol. Diagnosis* 14 (1973) 43.
- BARTLEY O. Patologisk formelstraktion registrerad med elektrokymografi. (In Swedish.) Paper read at the meeting of the Northern Association of Radiology, Gothenburg, June 1950.
- Electrokymographic changes in myocardial infarction. *Acta radiol.* 54 (1960) 81.
- The isometric relaxation phase of the left ventricle. *Acta radiol.* (1960) Suppl. N. 198.
- DAVIS S. The ventricular pulsations in myocardial infarction: a fluoroscopic and kymographic study. *Dis. Chest* 27 (1955) 287.
- PALLIN D. H. and SIEGMAN M. L. A comparison of electrokymography and roentgenkymography in the study of myocardial infarction. *Circulation* 1 (1950) 41.
- FROBERG A. und PILL Z. Über die Blutdrucksenkung bei der akuten Ischämie des Myokards. *Arch. Internat. Forsch.* 27 (1957) 54.
- GILLICK F. G. and REYNOLDS W. F. Clinical application of electrokymography. *Calif. Med.* 70 (1949) 407.
- HENRY G. C. and BOONE B. R. Electrocardiograph for recording heart motion utilizing the roentgenoscope. *Amer. J. Roentgenol.* 54 (1945) 217.
- LEHMAN A. A. and FLEISCHNER F. G. Dynamics of left atricle in mural left ventricular fluorocardiographic study. *Amer. J. Med.* 4 (1948) 791.

- RUBIN U. Electrolymography. With special reference to valvular pulmonary and infundibular stenosis. *Acta radiol.* (1956) Suppl. No. 134.
- SCHWEDER J. B., SAMET P. and MADDOCK H. Electrolymographic studies of relationship between electrical and mechanical events of cardiac cycle. *Proc. Soc. exp. Biol. Med.* 75 (1950) 591.
- TATOOLES C. and RANDALL W. Local ventricular bulging after acute coronary occlusion. *Amer. J. Physiol.* 201 (1961) 451.
- TEMMANT R. and WOODS C. The effect of coronary occlusion on myocardial contraction. *Amer. J. Physiol.* 112 (1935) 351.
- TUMANOVSKY M. N., HARMACH V. Y. and NOVISON Y. G. Electrolymographic study of the dog heart under normal conditions and after experimentally induced myocardial infarction. *Ter. Arkh.* 33 (1961) 11.
- ZIMMER JR. H. F., KAY C. F. and BENJAMIN JR. J. M. The electrolymograph: Studies in record and fidelity. *Circulation* 2 (1950) 197.

CORRUGATED VOCAL CORDS

A HENNINGSSON

The upper surface of the vocal cord is usually smooth. The increasingly common employment of laryngography has however disclosed a groove on this surface in the frontal projection in normal cases on phonation (BRINDLE 1967, BRINDLE & STELL 1968, JING 1970, LANDMAN 1970). BRINDLE (1967) called this the corrugated vocal cord. He pointed out that the groove is observed only when the central beam is exactly parallel with the upper surface of the vocal cord, which means that it may appear only on one vocal cord.

The cause of this normal corrugation is not clear. On phonation the vocal cord becomes longer owing to the fact that the distance between its points of attachment on the thyroid and cricoid cartilages increases. This extension of the cord takes place by contraction of the cricothyroid muscle (PERNAKOFF 1952) which also contributes to vocal cord adduction (ARNOLD 1961, TANABE *et coll* 1972). The cords are firmly anchored to the cricoid cartilage and trachea however by a ligamental membrane known as the conus elasticus. Phonation of a high tone may therefore possibly lead to a depression of the upper surface of the cord above the attachment of this ligament (Fig. 1). This mechanism of the origin of corrugation has been suggested by BRINDLE (1967).

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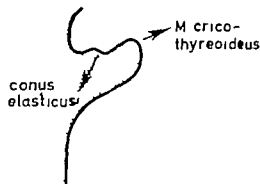


Fig. 1 Possible cause of corrugation of vocal cord by interaction between cricothyroid muscle and conus elasticus

A revision of a material of laryngographies often disclosed this corrugation in normal cases as well as in a few cases of vocal cord tumours. It was also particularly common though less marked in vocal cord paralyses.

The material comprised 112 consecutive cases examined during a 2 year period. The age and sex distributions have been previously presented (HENNINGSSON 1972). The diagnoses as verified at laryngoscopy appear in the Table. Laryngography was performed by the method of POWERS *et coll.* (1957) after premedication with 1 mg atropine subcutaneously.

Corrugated vocal cords were present in about a quarter of all cases (Table). They occurred in almost half of the normal cases (9/19) and still more frequently in cases with vocal cord paralysis (10/16). Those with corrugated vocal cords failed to differ from the total material as regards the age and sex distributions.

Table
Number of cases with corrugated vocal cords (absolute figures and percentages)

Diagnosis	No. of cases	Per cent
Normal	9/19	47
Paralysis	10/16	62
Oedema/fibrosis	6/32	19
Tumour	5/45	11
Total	30/112	27



Fig. 2 Normal case with corrugation of both vocal cords (→) Ap. laryngography during phonation

Discussion

It is important to be aware of this corrugation as a relatively frequent normal variation (Fig. 2) and of the fact that it may sometimes be present in only one vocal cord (Fig. 3). The groove may be differentiated from an early neoplasm by the fact that the latter causes thickening, is often visible in the lateral projection and protrudes into the lumen of the larynx on inspiration (BRUNDLE 1967). A corrugated vocal cord may of course occur in combination with malignancy (Fig. 4).

The frequency of corrugated vocal cords in vocal cord paralysis is worthy of note. Corrugations were evident in both unilateral (Fig. 5) and bilateral (Fig. 6) paralyses and occurred both on phonation (Fig. 6 a) and on respiration (Fig. 6 b). These paralyses were due to a lesion of the inferior laryngeal nerve (recurrent nerve) in 5 cases while in the other cases the cause was unknown. The cricothyroid muscle, the contraction of which possibly gives rise to this groove in the upper surface of the vocal cord by an interaction with the elastic cone (Fig. 1) is on the other hand innervated by the superior laryngeal nerve (TAMARÉ et coll. 1972). In paralysis of the recurrent nerve a reflex contraction of the cricothyroid muscle takes place resulting among other things to adduction of the cord from an intermediary to a paramedian position (TSCHIASANY 1957). This has been confirmed by section of the superior laryngeal nerve after which the paralysed cord became abducted to an intermediary position (FREEDMAN 1956, TSCHIASANY 1957). The reflex contraction of the cricothyroid muscle in recurrent laryngeal nerve paralysis may thus possibly explain why a corrugated vocal cord so often occurs in this condition.



Fig. 3



Fig. 4



Fig. 5

Fig. 3 Normal case with corrugation of left vocal cord (\rightarrow) A.p. laryngography during phonation

Fig. 4 Transverse section of left vocal cord (\longleftrightarrow) and corrugation of both vocal cords (\rightarrow) A.p. laryngography during phonation

Fig. 5 Right recurrent laryngeal nerve paralysis. Corrugated vocal cord on the paralyzed side (\rightarrow) A.p. laryngography during phonation

The fact that a groove in the upper surface is not rare when a vocal cord is paralysed therefore supports the hypothesis of BARNILE (1967) that it lies above the attachment of the conus elasticus in the cord and is due to an interaction between the cone and the cricothyroid muscle. When a corrugation is present in the paralysed cord this may therefore indicate that the paralysis is due to a lesion of the inferior laryngeal nerve (recurrent) below the origin of the superior laryngeal nerve from the vagus nerve.



Fig. 6 Bilateral recurrent laryngeal nerv. paralysis. Corrugated vocal cords on both sides (→) evident during both phonation (a) and respiration (b).

SUMMARY

A groove in the upper surface of a vocal cord may sometimes occur as a normal variation. This finding was evident in almost half the normal cases in material of 112 cases and even more frequently in those with vocal cord paralysis. The origin of the corrugation and its diagnostic importance especially in localizing the level of the nerve lesion in vocal cord paralysis is discussed.

ZUSAMMENFASSUNG

Eine kleine Kerbe in der Oberfläche des Stimmbandes wird oft als eine Variante beobachtet. In einem Material von 112 Fällen wurde dies in beinahe der Hälfte der Fälle beobachtet. In Fällen von Stimmbandlähmung sogar häufiger. Der Ursprung dieser Wellenbildung und deren diagnostische Bedeutung, besonders bei der Lokalisierung der Ursache der Stimmbandlähmung, wird besprochen.

RÉSUMÉ

Une gouttière à la surface supérieure d'une corde vocale peut parfois être une variation normale. Ce signe est trouvé dans près de la moitié des cas sur une série de 112 sujets normaux et il est trouvé encore plus souvent chez les sujets atteints de paralysie des cordes vocales. L'auteur étudie l'origine de ce plissement et son importance diagnostique en particulier pour localiser le niveau de la lésion nerveuse dans la paralysie des cordes vocales.

REFERENCES

- ARNOLD G. E. Physiology and pathology of the cricothyroid muscle. *Laryngoscope* (St. Louis) 71 (1961) 687.
- BRINDLE M. J. The corrugated vocal cord. *Amer. J. Roentgenol.* 101 (1967) 839.
- and STELL P. M. Radiological assessment of laryngeal carcinoma. *Clin. Radiol.* 19 (1968) 257.
- FREEDMAN L. M. The role of the cricothyroid muscle in tension of the vocal cords. *Laryngoscope* (St. Louis) 66 (1956) 574.
- HÄMMINGSSON A. Roentgenologic examination of the larynx. A clinical comparison. *Acta radiol. Diagnosis* 12 (1972) 433.
- JING B. S. Roentgen examination of the larynx and hypopharynx. *Radiol. Clin. N. Amer.* 8 (1970) 361.
- LANDMAN G. H. M. Laryngography and cinelaryngography. *Excerpta Medica Foundation* Amsterdam 1970.
- PERKHOFF E. *Topographische Anatomie des Menschen*. Vol. 3. Urban & Schwarzenberg, Wien 1952.
- POWERS W. E., MCGEE H. H. and SKAMAN W. B. Contrast examination of the larynx and pharynx. *Radiology* 68 (1957) 169.
- TANABE M., IISHI N. and KITAJIMA K. Vibratory pattern of the vocal cord in unilateral paralysis of the cricothyroid muscle. *Acta oto-laryng.* 74 (1972) 339.
- TSUCHIYAMA K. Therapeutically induced paralysis of the cricothyroid muscle or its removal in paralytic laryngeal stenosis. *Arch. Otolaryng.* 65 (1957) 133.

SALPINGITIS ISTHMICA NODOSA DEMONSTRATED BY HYSTEROSALPINGOGRAPHY

M. LEA THOMAS and D. H. ROSE

Salpingitis isthmica nodosa is the descriptive term for nodular thickening of the isthmic portion of one or both fallopian tubes. The interstitial portion of the adjacent uterine cornu may also be involved (BENJAMIN & BEAVER 1951). The nodules vary in size from microscopic to several centimetres in diameter.

The name salpingitis isthmica nodosa was first introduced by CHIARI (1887). Other terms which have been used for the condition include adeno-myosalpingitis (MEYER 1903, RABINOVITZ 1913), endosalpingiosis (SAMPSON 1930) and diverticulosis of the fallopian tubes (SCHENCKEN & BURNS 1943). These various terms reflect the uncertain aetiology of the condition.

Several theories of the pathogenesis of salpingitis isthmica nodosa have been postulated: congenital (VON RECKLINGHAUSEN 1896), inflammatory (CHIARI 1887, RABINOVITZ 1913, FRANKL 1929, SAMPSON 1930, SCHENCKEN & BURNS 1943), hyperplasia (BARES 1927) and developmental, similar to adenomyosis uteri (BENJAMIN & BEAVER 1951). JEFFCOATE (1967) states that the condition is most likely to be a manifestation of endometriosis or salpingiosis rather than inflammation.

Histologically the lesion appears to begin as a proliferation of the normal



Fig. 1. a) Early film. Bilateral salpingitis isthmica nodosa. b) Later film. Filling of bilateral hydrosalpinges. Only a little peritoneal spill from left tube.



Fig. 2. a) Early film. Bilateral salpingitis isthmica nodosa. b) Later film. Left hydrosalpinx. Free spill of contrast from both tubes.

epithelium of the isthmus of the tube. This epithelium penetrates the myosalpinx to form a labyrinth of gland-like spaces connected to the tubal lumen. There is



b

Fig. 3 a) Early film Bilateral salpingitis isthmica nodosa conglomerating to form masses
b) Later film Bilateral free spill of contrast

secondary hypertrophy and hyperplasia of the surrounding myosalpinx which may occlude some of the ramifying canaliculi causing their dilatation and making them susceptible to secondary infection (BENJAMIN & BEAVER 1951)

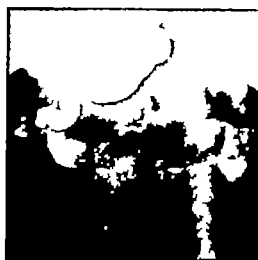
Salpingitis isthmica nodosa causes no symptoms other than infertility which is often investigated by hysterosalpingography

Most descriptions have been based on operative or post mortem material and there have been few radiologic reports of the condition (MILLS et coll 1968)

Therefore it seemed appropriate to describe the radiologic appearances of salpingitis isthmica nodosa at hysterosalpingography in 7 patients and to present a simplified technique of performing the investigation

Case reports

Case 1 A 34 year old Jamaican was admitted with a 4 year history of secondary infertility. On physical examination no abnormality was found. Tubal insufflation was equivocal. At hysterosalpingography there were changes of bilateral salpingitis isthmica nodosa and bilateral hydrosalpinges with no spill of contrast medium into the peritoneal cavity on the right and only a little on the left (Fig. 1)



b

Fig 4 a) Early film Bilateral salpingitis isthmica nodosa with right hydrosalpinx. Enlarged irregular uterus suggesting fibroid b) Delayed film ten minutes later. A little delayed peritoneal spill on the right



b

Fig 5 a) Early film Bilateral salpingitis isthmica nodosa. Anteverted uterus b) Later film. Little peritoneal spill from both tubes. Uterus shown en face by traction on vulsellum forceps

Case 2 A 31 year old West Indian was admitted with history of 10 years secondary infertility. Five years before admission right hydrosalpinx and occlusion of the left tube had been found at hysterosalpingography. A right salpingostomy was performed. However she failed to conceive and at repeat examination she was found to have salpingitis isthmica nodosa with bilateral free peritoneal spill of contrast medium and a left hydrosalpinx (Fig 2).



Fig 6 a) Early film Salpingitis isthmica nodosa shown on left side only b) Later film Salpingitis isthmica nodosa now show bilaterally Only little spill from right tube

Case 3 A 24 year old Jamaican was admitted with a history of 25 years secondary infertility. She had previously had a normal full term delivery. Earlier in the year of admission she had had an attack of acute right salpingitis treated with antibiotics.

Bilateral salpingitis isthmica nodosa with patent fallopian tubes and free spill of contrast medium on both sides was demonstrated at hysterosalpingography (Fig 3).

Case 4 A 36 year old Jamaican was admitted with 6 years secondary infertility. She had had two normal pregnancies which had been followed by 4 miscarriages at 6 weeks gestation. Three of these abortions were followed by dilatation and curettage. Four years before this admission a laparotomy was performed for uterine enlargement and she was found to have fibroids. In addition the left fallopian tube was fixed by multiple pelvic adhesions and there was a small left hydrosalpinx. A left salpingostomy was performed. Nodules of endometriosis were found in the pelvic peritoneum.

At hysterosalpingography 4 years after this operation right sided salpingitis isthmica nodosa and bilateral hydrosalpinges were demonstrated with a little spill of contrast medium on both sides. The appearances also suggested uterine fibroids.

Case 5 A 30 year old Jamaican was admitted with a history of 10 years secondary infertility. Her first pregnancy ended at 30 weeks gestation. There was no known puerperal complications. On pelvic examination she had a bulky swelling at the right cornu of the uterus considered likely to represent a fibroid.

At hysterosalpingography it was found to have bilateral salpingitis isthmica nodosa with right hydrosalpinx. The left tube was occluded. The uterus was greatly enlarged presumably by fibroids (Fig 4). There was a little delayed spill of contrast medium on the right.

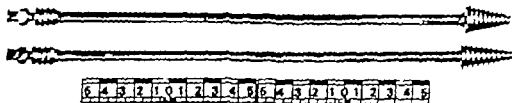


Fig. 7. Leech-Wilkinson cannula screw tipped olive in situ.

As this patient was sickle cell prelude a general anaesthetic was not given and the uterine examination was carried out under basal sedation.

Case 6. A 28-year-old Maori woman was admitted with primary infertility. She had had pulmonary tuberculosis treated in the past but no history of a gynaecological disorder. On examination no abnormality was found. At hysterosalpingography there was bilateral salpingitis tubum nodosa but both fallopian tubes were patent although contrast medium did not pull freely on either side (Fig. 6).

Case 7. A 32-year-old Chinese woman was admitted with primary infertility. She was found to have right tubal swelling. On examination:

At hysterosalpingography there was bilateral salpingitis tubum nodosa. There was no evidence of occlusion of the left tube beyond the nodular part and only a little spill on the right (Fig. 6).

Technique

We perform hysterosalpingography under light general anaesthesia. If this is contraindicated however basal sedation is given. The examination is carried out in an outpatient basis and the patient is allowed to leave the department after full recovery.

After being placed in the lithotomy position at the end of a screening table equipped for television fluoroscopy the perineum and vagina are cleaned with Cetrimide solution BPC. A vaginal examination is performed and a Sims speculum inserted into the vagina. The anterior lip of the cervix is gripped by a vulsellum forceps and a Leech-Wilkinson cannula (Fig. 7) attached to a syringe and already filled with contrast is inserted into the cervical canal and rotated to obtain a tight fit. The speculum is removed and the patient placed supine on the screening table. The abdomen is briefly screened for calcification or any other abnormality. Whilst pulling on the vulsellum forceps to overcome any anteversion or retroversion of the uterus up to 20 ml of the contrast medium Urografin 16% is injected by hand under intermittent screen control. Two films are taken as a routine one to show the fallopian tubes and the other to demonstrate

Table
Findings at hysterosalpingography

Case N	Salpingitis isthmica nodosa	Hydrosalpinx	Tubes patent (P) or occluded (O)		Degree of peritoneal spill (F = fr D = dismantled)		Additional findings
			Right	Left	Right	Left	
1	P lateral	B lateral	O	P	O	D	—
2	B lateral	Left	P	P	F	F	—
3	B lateral	—	P	P	F	F	—
4	Right	Bilateral	P	P	D	D	F broad
5	B lateral	Right	P	O	D	O	F broads
6	B lateral	—	P	P	D	D	—
7	B lateral	—	P	O	D	O	—

peritoneal spill The uterus is seen in two positions by moving the vulsellum forceps This also gives an indication of the uterine mobility An endometrial biopsy may be taken if indicated The whole examination takes about 20 minutes to perform including induction of anaesthesia

Results

The findings in the seven patients are shown in the Table The appearances of salpingitis isthmica nodosa as found at these examinations are well defined punctate accumulations of contrast medium collecting around the isthmus of the fallopian tubes and filling from the tubal lumen as the contrast medium is introduced (Fig 3) In all our cases the most medial part of the tube appeared normal but this normal segment varied in length from a few millimetres (Fig 3) to several centimetres (Fig 4) In some instances only a few tubal diverticula filled with contrast medium (Fig 6) whilst in others numerous diverticula formed a sizeable mass (Figs 4-6) which was palpable per vaginam in one patient (Case 7 Fig 6) In no examination was there radiologic evidence of involvement of the uterine cornua

Discussion

The importance of salpingitis isthmica nodosa is that it causes infertility in about half the patients affected (ANDERSON 1966)

Over a period of 18 months 200 women were examined by hystero-salpingography for infertility in our department From this total the 7 patients with radiologic evidence of salpingitis isthmica nodosa in this series were encountered

giving an incidence of 3.5 %. This compares with the series of MILLS *et coll* (1968) who reported an incidence of 2.8 % in 364 examinations.

About one third of our patients investigated nowadays are of non Caucasian immigrant stock and all seven patients in our series fell into this group 5 of them being West Indian. This is in keeping with the high incidence of the condition in negroes reported by SCHENKEN & BURNS (1943) and BENJAMIN & BEAVER (1951).

In only one case (Case 7 Fig 6) might it have been possible to consider the diagnosis before hysterosalpingography because a right tubal swelling was found on pelvic examination. Two patients (Cases 2 and 4) had undergone gynaecologic surgery a few years before hysterosalpingography and no evidence of salpingitis isthmica nodosa was found in either although pelvic endometriosis was seen in one (BENJAMIN & BEAVER 1951).

The radiographic features of salpingitis isthmica nodosa in our series are essentially similar to those described by others (MILLS *et coll* 1968).

The condition was bilateral in 6 of our 7 patients (86 %). Of the 10 patients in the radiologic series of MILLS *et coll* 6 (60 %) had bilateral involvement whilst BENJAMIN & BEAVER reported bilateral disease in 35 % of the cases they examined pathologically. The high incidence of hydrosalpinges, tubal occlusions and apparently reduced spill of the contrast medium into the peritoneal cavity in addition to the salpingitis isthmica nodosa in this series suggests that inflammation commonly accompanies the disease and may be contributory to the patient's infertility.

For hysterosalpingography we use a light general anaesthesia as a rule as this allows a more thorough pelvic examination to be carried out at the same time and is preferred by the patients. It may also contribute to the absence of tubal spasm as we have not encountered this as a cause of obstruction. We have had no significant complications from either the anaesthetic or the procedure in over a thousand patients. When there is a contraindication to general anaesthesia such as a positive sickle cell test (Case 5) basal sedation is used.

We have found the Leech Wilkinson cannula (Fig 7) most convenient for the examination as the ridged screw threaded conical olive available in two sizes allows a close fit of the tip into the cervix in the majority of patients. Even a patulous os can usually be narrowed by a use of a vulsellum forceps so that a water tight connection can be obtained. When cervical incompetence is clinically suggested or a close fit with a Leech Wilkinson cannula cannot be obtained, we use the Malmstrom Westman cannula.

We prefer to use the water soluble contrast medium Urografin 76 which has a relatively low viscosity with a high iodine content. It passes readily through the fallopian tubes into the peritoneal cavity if these are patent so that immediate

results can be obtained. The presence of a hydrosalpinx can be confirmed by a delayed film at 10 minutes if necessary (Fig. 4). In our opinion the disadvantages of oily contrast medium venous intravascular the long interval which must be allowed before peritoneal spill can be demonstrated with certainty and foreign body reactions (Brown et coll. 1949) outweigh the advantages of good contrast possible therapeutic value and the absence of abdominal pain.

A television screening technique is always used nowadays as films can be taken at the appropriate incident to confirm the findings of fluoroscopy. By screening it is possible to ensure that the uterus and fallopian tubes have been diagnostically filled with contrast medium the degree and site of spill of the medium into the peritoneal cavity can be seen and the mobility of the uterus observed. The uterus can be exposed en face and in profile by movement of the vulvillum forceps attached to the cervix.

Less than 1 minute's screening time is necessary for the examination. The use of an image intensifier considerably reduces gonadal radiation and a further reduction can be obtained by employing an automatic exposure device which ensures that repeat films are not required for technical reasons.

All the examinations in this department are carried out by the radiologic staff.

SUMMARY

The radiologic appearances of salpingitis isthmica nodosa at hysterosalpingography are described in seven patients. The appearances consist of punctate accumulations of contrast medium around the isthmus portion of the fallopian tubes. The condition is usually bilateral and other tubal abnormalities may be present. All the patients in this series complained of infertility and all were of non-Caucasian extraction. A simple technique for hysterosalpingography is described.

ZUSAMMENFASSUNG

Das roentgenologische Bild der Salpingitis isthmica nodosa bei der Hysterosalpingographie wird bei sieben Patienten beschrieben. Das Bild besteht aus punktförmigen Ansammlungen von Kontrastmittel um den Isthmus tubae uterinae. Das Vorkommen ist gewöhnlich bilateral und es können andere Veränderungen der Tuben vorhanden sein. Alle Patienten dieser Serie litten an Infertilität und waren von nicht kaukasischer Herkunft. Eine einfache Technik der Hysterosalpingographie wird beschrieben.

RÉSUMÉ

Description des aspects radiographiques de la salpingite isthmique noueuse à l'hysterosalpingographie. Les images consistent en accumulations punctuées de moyen de contraste autour de la partie isthmique des trompes de Fallope. Cette affection est habituellement bilatérale et d'autres anomalies tubaires peuvent exister. Toutes les malades de cette série étaient atteintes de stérilité et n'étaient pas d'origine blanche. Les auteurs décrivent une technique simple d'hysterosalpingographie.

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REFERENCES

- ANDERSON W A D Pathology Fifth edition p 1167 C V Mosby Co St Louis 1966
- BARNES A Nouvelle étude sur la nature de la salpingite nodulaire Gynécologie 26 (1977) 400
- BENJAMIN C L and BEAVER D C Pathogenesis of salpingitis isthmica nodosa Amer J clin Path 21 (1951) 212
- BROWN W E JENNINGS A F and BRADBURY J T The absorption of radiopaque substances used in hysterosalpingography Amer J Obstet Gynec 58 (1949) 1041
- CITELLI H Zur pathologischen Anatomie des Eileiterscatarrhs Z Heilkunde 8 (1887) 457
- FRANKE O Salpingitis isthmica nodosa und Adenomyosis tuba Arch Gynak 135 (1929) 556
- JEFFCOATE T V A Principles of gynaecology Third edition p 413 Butterworths London
- MEYER R Über adenomatöse Schleimhautwucherungen in der Uterus und T. bewand und ihre pathologisch anatomische Bedeutung Virchows Arch pat Anat 172 (1904) 304
- MILLS J UPADHAYAY P P and CAESTARS L S Diverticulous of the fallopian tubes—salpingitis isthmica nodosa Clin Radiol 19 (1968) 233
- RAHMOVITZ M The pathogenesis of adenomyosalpingitis (salpingitis nodosa) Report of 10 cases Amer J Obstet Dis Wom 68 (1913) 711
- ON RECKLINGHAUSEN Die Adenomyome und C. stadenome der Uterus und T. bewand Berlin 1896 (Cited by Rahmovitz)
- SAMSON J A Post salpingectomy endometriosis (endosalpingiosis) Amer J Obstet Gynec 20 (1930) 443
- SCHENKEL J R and BURNS E L Study and classification of nodular lesions of the fallopian tubes salpingitis isthmica nodosa Amer J Obstet Gynec 45 (1943) 624

DYE DILUTION TECHNIQUE WITH ANGIOGRAPHY IN THE INVESTIGATION OF RENAL ARTERIOVENOUS SHUNTING

JAN GOTHILIN

Arteriovenous shunting in the kidney occurs mainly in traumatic fistula haemangioma and carcinoma. The blood flow through the renal parenchyma, which is of decisive importance for renal function, may be reduced in such cases. It was therefore thought worth while to investigate the distribution of flow in kidneys with arteriovenous shunts.

Material and Methods Arteriovenous shunting was revealed by nephroangiography in 12 patients, 2 of whom had haemangiomas, 4 fistulas following renal biopsy and 6 carcinomas. Renal blood flow was determined by a dye dilution technique in direct connection with nephroangiography (GOTHILIN & OLIN 1970, 1973). If possible the distribution of flow between the shunt and the parenchyma was determined separately (EKLUND et al. 1972).

Submitted for publication 23 February 1972

Table 1

Arteriovenous shunts due to renal biopsy in cases 1 to 4 and haemangiomas in cases 5 and 6

Case	Age	Sex	S	RAD	RBF	SBF	RBF/m	SBF/m	VV _p
1	22	F	R	4.5	87	8	63	6	24
2	17	M	R	5.0	580	805	530	435	26
3	32	F	R	6.4	1103	821	645	480	—
4	18	M	R	4.1	330	—	202	—	51
				4.1	585	317	560	595	44
5	31	F	R	4.0	346	12	225	8	47
				5.5	629	209	348	115	74

S Side of kidney examined

RBF Total renal blood flow (ml/min)

SBF Blood flow through the shunt (ml/min)

RBF/m Renal blood flow (ml/min/m² body area)SBF/m Shunt flow (ml/min/m² body area)VV_p Vascular volume (ml) of parenchyma

Results

The dye dilution curves in all cases of fistula and haemangioma consisted of two components that could easily be demarcated and treated to yield blood flow and related parameters. The curves from the tumour cases could not be separated into two components.

Values obtained from the two patients with haemangioma and the 4 patients with fistulas after renal biopsy are presented in Table 1. Angiography in Case 1 (histology amyloidoma) revealed small kidneys, thin and tortuous renal arteries and a poor nephrographic phase in the cortex. Two small fistulas lay in the lower pole. The renal blood flow, 9 per cent of which constituted the shunt flow, was much decreased. The dye appeared somewhat earlier in the renal vein of this kidney than in that on the contralateral side.

Case 2 (clinical diagnosis subchronic glomerulonephritis biopsy specimen not representative) was one of hypertensive disease. Angiography demonstrated

Table 1 (cont.)

Case	VR _p	VR	MTT _p	MTT	AT	Diagnosis
13	63	498	19.1	10.1	3.7	Amyloidosis
32	46	10	9.1	2.4	0.3	Subcapsular glomerulonephritis
73	22	65	—	3.4	0.1	Chronic interstitial nephritis
—	18	—	9.2	—	2.6	Haematuria renal biopsy not representative
22	21	18	9.7	4.2	0.4	Haematuria renal biopsy not representative
8	16	435	8.2	4.1	1.4	Haemangioma
18	14	28	10.5	5.3	0.2	Haemangioma
VR	Vascular volume (ml) of shunt					
VR _p	Vascular resistance (peripheral resistance units) of parenchyma					
VR _s	Vascular resistance (peripheral resistance units) of shunt					
MTT	Mean transit time (seconds) for parenchyma					
MTT	Mean transit time (seconds) for shunt					
AT	Appearance time of dye in the renal vein after passage through shunt					

two arteriovenous fistulas in the lower pole of the right kidney and a reduction in the amount of the parenchyma peripherally. The shunt flow constituted 82 per cent of the total renal blood flow. The appearance of the dye was 0.3 s compared with about 2.5 s in the parenchyma.

Angiography in Case 3 (histology: chronic interstitial nephritis) demonstrated a small kidney with cortical scars and a large shunt with a poor nephrographic phase in the cortex peripherally. The arteries were narrow and tortuous consistent with the histology. The shunt flow amounted to 74 per cent of the total flow. The appearance time of the dye 0.1 s was the shortest of any of the cases.

Case 4 had haematuria (clinically probably acute glomerulonephritis but biopsy specimen not representative). Angiography revealed two renal arteries the dorsal one of which supplied a large fistula as well as changes consistent with acute glomerulonephritis. The mixing of blood and dye was poor so that the values for the renal blood flow were unreliable but the appearance time of the



Fig 1 Case 6 Haemangioma a) Angiography of the right kidney b) Dilution curve Early appearance time of the dye the concentration maxima and the semilogarithmic plot of the shunt component are evident

dye was however short. The shunt flow was estimated to comprise 54 per cent of the flow determined by dye injection into the dorsal artery.

Urography in Case 5 disclosed a movable right kidney and angiography a small haemangioma. The shunt flow made up 3.5 per cent of the total renal blood flow. The appearance time of the dye was 1.4 s compared with about 2.4 s for the parenchyma.

Angiography in Case 6 (Fig 1) demonstrated a large haemangioma situated centrally in the upper pole of the right kidney. The pole was smaller than usual but no cortical scars were evident. The arteries peripheral to the shunt were narrow and tortuous. The shunt flow formed 33 per cent of the total blood flow through the kidney. The appearance time of the dye was 0.2 s as compared with about 3 s for the parenchyma.

A richly vascularized carcinoma 8 cm \times 11 cm in size was present in Case 7 (Table 2). The flow was very high i.e. 2800 ml/min. The distribution of blood between the carcinoma and the parenchyma could not be assessed as the

Tabl 2

Carcinomas arranged according to the magnitude of the renal blood flow.

Case	Age	Sex	S	RAD	RBF	RRF/ m	VA	VR	VTT	AT	Tumour size (cm)	AT in contra lateral kidney
7	77	F	L	7.5	2824	1618	90*	3	6.3	0.2	8 × 11	4.3
8	54	M	L	8.3	2593	1320	363	3	8.5	0.1	12 × 12	
9	73	M	L	7.1	860	450	128	10	8.9	2.2	7 × 11	
10	55	M	L	6.8	557	310	90	19	9.4	0.3	11 × 16	3.8
11	44	F	R	3.3	446	283	96	19	12.9	1.7	4.5 × 5	
12	70	M	L	3.8	354	161	68	5.5	12.3	2.1	2 × 3	

S Side of kidney examined

RBF Total renal blood flow (ml/min)

RRF/m Renal blood flow (ml/min/m body area)

VA Vascular volume (ml)

VR Vascular resistance (peripheral resistance units)

VTT Vascular transit time (seconds)

AT Appearance time (seconds)

two dye dilution curves were completely superimposed. The vascular volume was high and the vascular resistance low while the appearance time of the dye was 0.2 s. The diameter of the renal artery was as much as 7.5 mm (normal value according to GOTHLM & OLIN 5.4 mm, range 4.3 to 6.8 mm); early filling of the renal vein could be demonstrated. The findings in Case 8 (Fig. 2) were similar to those in Case 7.

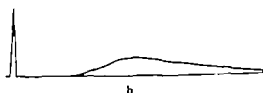
The tumours in Cases 11 and 12 were small. The renal blood flow was normal in Case 11 and below normal in Case 12. The appearance time of the dye was shorter than usual but there was also no early filling of the renal veins.

Discussion

The reliability of the dye dilution method has been discussed in a previous paper (GOTHLM & OLIN 1973) and the calculation of the flow through shunts has also been dealt with elsewhere (EARLEND *et al.* 1972). The present concentration curves were similar in a series of examinations, indicating that the method is a reliable one for the determination of shunt flow. Use of an indicator dilution technique is often the easiest means of estimating shunt flow, even if other techniques be available. If each of the two vascular territories be of large volume, however, as in a richly vascularized carcinoma, the two flow components of the concentration curve are inseparable. That shunting exists in carcinomas was



Fig 2 Case 8 Carcinoma of the left kidney a) Angiography Extensive pooling of contrast medium b) Dye dilution curve of low peak height after injection of 10 ml dye Early appearance time



proved by the short appearance time of dye in the renal vein and at angiographic examination of the two largest carcinomas by the early appearance of contrast medium in the renal vein

Fistulas consequent upon renal biopsy are not uncommon (EÄRLUND & INDHOLM 1971 MENDO & ELAIN 1971 among others) MALLOY et coll (1967) reviewed the literature on haemangiomas and by adding three of their own, increased the total number described to 27

Large fistulas are revealed by angiography but smaller ones may be impossible to detect except by an indicator dilution technique as EÄRLUND et coll (1972) demonstrated in rabbits It is possible that in man smaller haemangiomas

may go undetected at angiography yet be revealed by a dye dilution examination and thereby explain for example haematuria

Haemodynamic investigations of renal arteriovenous fistulas have been performed by SCHIFFLEY et coll (1959) and by MALDONADO et coll (1964) by means of an indicator dilution technique with measurement of the recirculation time in large central vessels or the brachial artery. FOX & WOOD (1957) considered that the blood flow in the renal vessels in cases of arteriovenous fistulas might be assessed by selective catheterization and an indicator dilution technique; this appears never to have been done. MALDONADO et coll demonstrated renal ischaemia distal to a fistula by nephrography and separate clearance determinations. IROGARDI et coll (1971) published 4 cases of renal arteriovenous fistulas in which the flow was determined by a dye dilution technique. Clearance determinations were performed in 2 of these cases.

Only a rough conception of the flow peripheral to the fistula can be obtained by angiography in the presence of arteriovenous shunting. The function of the renal parenchyma as opposed to the kidney as a unit may only be measured if clearance determination be combined with calculation of the blood flow through the fistula and the parenchyma, respectively. To calculate the function of the renal parenchyma, correction must be made for the shunt flow in the following way. If the concentration of ^5Cr EDTA or ^{131}I Hippuran in the artery be A and in the veins after passage of the parenchyma B and in the main renal vein B_1 , the total extraction E_t will be

$$E_t = \frac{A - B_1}{A - b}$$

and the extraction by the parenchyma E_c will be

$$E_c = \frac{A - B}{A - b}$$

where b is the activity of the background.

The total flow through the kidney F_t is

$$F_t = F + F_p$$

where F = shunt flow and F_p parenchymatous flow.

Thus $B_1 \times F = B \times F + A \times F$ and the concentration of the substance after passage through the parenchyma will be

$$B_2 = \frac{B_1 \times F - A \times F}{F}$$

Solution of the equations yields

$$E_c = \frac{F_t}{F} \times E_t$$

That is, the extraction by the parenchyma is equal to the ratio between the total flow and that through the parenchyma, multiplied by the total extraction by the kidney

LINGGARDH *et coll* (1971) determined the total blood flow by a dye dilution technique in two kidneys with arteriovenous fistulas after renal biopsy and also determined the extraction by the kidney of ^{51}Cr EDTA and PAH. They published the following table

Case	Cr EDTA				PAH			
	Extraction ratio		Clearance		Extraction ratio		Clearance	
	AV	C lat	AV	C lat	AV	C lat	AV	C lat
1	0.029	0.083	4.6	10.3	0.069	0.159	19	26
3	0.036	0.108	9.7	13.7	0.116	0.435	31	33

If these values be corrected for the shunt flow with the formula described above the following results are obtained

Case	Cr EDTA				PAH		
	F_t/F	E_t	E_p	E_{ct}	E_t	E_p	E_{ct}
1	281/90	0.029	0.091	0.063	0.069	0.278	0.159
3	413/163	0.036	0.091	0.106	0.116	0.294	0.435

Abbreviations: AV = kidney with arteriovenous fistula; C lat = contralateral kidney; F_t = total flow through the kidney; F = flow through the parenchyma; E_t = total extraction; E_p = extraction by the parenchyma; E_{ct} = extraction by the contralateral kidney.

The parenchyma of the kidney with the arteriovenous fistula in Case 1 had at least as good a function as that of the contralateral kidney. The difference in the extraction of ^{51}Cr EDTA between the two kidneys in Case 3 is small. The PAH values in Case 1 indicated a better tubular secretion in the kidney with a lesion than on the contralateral side while the reverse was evident in Case 3. The differences may be ascribable to poor mixing of the blood in the renal vein. The decreased clearance in these two kidneys is thus dependent not upon a decreased function of the parenchyma *per se* but upon a reduction in the blood flow through it. The clearance does not demonstrate the potential of the parenchyma. If the parenchymatous flow be reconstituted whether by spontaneous coagulation or by operation of the fistula, an improved total function is to be expected.

OFSTAD & KOLSAER (1970) demonstrated by angiography a prolonged appearance time and a decreased concentration of contrast medium in the parenchyma in renal carcinoma. LINGGARDH & LUNDSTROM (1971) reported a prolonged appearance time by means of a dye dilution technique in a case of adenocarcinoma and attributed this to hypoperfusion of the renal parenchyma. The appearance time of the dye in the present investigation was shorter than normal (normal value mean 2.4 s). The mean transit time was also short in Cases 7, 8 and 9 but since it reflected the time for both the carcinoma and the parenchyma it was difficult to interpret. Early filling of the renal vein occurred in Cases 7 and 8. The contrast medium will pool more in carcinomas with large vessels and sometimes its appearance in the renal vein will be delayed; the same holds true for the dye. The large vascular volume of the carcinomas (Table 2) corresponds well with their appearances at angiography (Fig. 2).

The values of vascular resistance in parenchyma and shunt respectively indicate the resistance in coupled parallel circuits that is to say the shunt compared with about 10^6 capillaries coupled in parallel in the parenchyma. It may seem contradictory that the resistance in shunts may be higher than in the parenchyma, e.g. in Case 3, but according to the concept of parallel coupling of circuits this must be accepted.

The indicator dilution technique is very suitable for investigating the haemodynamics of shunts in kidneys. It is not time consuming and produces almost no discomfort if performed in connection with routine angiography. The examination may yield the information necessary to determine whether a fistula should be operated upon or not. It is easy to determine the cardiac output at the same time as the renal blood flow: the dye solution is injected into a central vein and sampling performed from a central artery. The main reason for operating upon fistulas seems to be the danger of cardiac failure (RIZO 1925; ADAMS 1951; MALDONADO *et al.* 1964) as well as decreased clearance due to the lowered perfusion of the parenchyma.

Acknowledgements

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SUMMARY

The haemodynamics of the kidney in 2 cases of haemangioma, 4 of fistulas after renal biopsy and 6 cases of carcinoma were investigated by a dye dilution technique in connection with routine angiography. The method is easy to perform and not stressful to the patient. The cardiac output may be determined at the same time.

ZUSAMMENFASSUNG

Die Hemodynamik der Niere wurde in 2 Fällen mit Hämangiomen 4 Fällen von Fisteln nach Nierenbiopsie und 6 Fällen von Karzinomen mit einer Farbstoffverdünnungstechnik im Zusammenhang mit Routineangiographien untersucht. Die Methode ist einfach auszuführen und wird nicht vom Patienten als unbeliäglich empfunden. Das Herzschlagvolumen kann gleichzeitig bestimmt werden.

RÉSUMÉ

Il a été étudié l'hémodynamique rénale dans 2 cas d'hémangiome 4 cas de fistule après biopsie rénale et 6 cas de cancer au moyen d'une technique de dilution de colorant associée une angiographie ordinaire. Cette méthode est d'exécution facile et est pas pénible pour le malade. Le débit cardiaque peut être déterminé en même temps.

REFERENCES

- ADAMS H. Congenital and acquired aneurysms. *Surg Gynec Obstet* 92 (1951) 663
- ERIKSSON L. GOTTLIN J. and OLIN T. Arteriovenous fistulae: rabbit kidney studied by dye dilution technique and by angiography. *Scand J Urol Nephrol* 6 (1972) 84
- and LUNDHOLM T. Arteriovenous fistulae following percutaneous renal biopsy. *Acta radiol Diagnosis* 11 (1971) 38
- FOX J. and WOOD E. Applications of dilution curves recorded from the right side of the heart or venous circulation with the aid of a new indicator dye. *Proc Mayo Clin* 32 (1957) 541
- GOTTLIN J. and OLIN T. Nefroangiografi kompletterad med blodflödesmätning, enligt färgspädningsmetoden. (In Swedish.) *Nord Med* 84 (1970) 1317
- Dye dilution technique with nephroangiography for the determination of renal blood flow and related parameters. *Acta radiol Diagnosis* 14 (1973) 113
- LINDGREN G. LINDQVIST B. and LUNDSTRÖM B. Renal arteriovenous fistula following puncture biopsy. In: Studies on separate renal blood flow and function using a dye-dilution technique and radiochemicals. *Scand J Urol Nephrol* (1971) Suppl. N. 8
- and LUNDSTRÖM B. Renal blood flow in man studied with a dye-dilution method. In: Studies on separate renal blood flow and function using a dye dilution technique and radiochemicals. *Scand J Urol Nephrol* (1971) 8 suppl. No. 8
- MALDONADO J. SHARP S. BERNATE P. et coll. Renal arteriovenous fistula: A reversible cause of hypertension and heart failure. *Amer J Med* 37 (1964) 499
- MALLOY T. LEHRMAN P. and MURPHY J. Renal arteriovenous fistula. *J Urol* 98 (1967) 40
- MENDOZA G. and FLICK M. Immediate angiographic manifestations of iatrogenic renal injury due to percutaneous needle biopsy. *Radiology* 100 (1971) 335
- OSTAD J. and HOLBAEKER L. Renal function studies: renal carcinoma. *Clin Sc* 30 (1970) 367
- RIZZI M. Abnormal arteriovenous communications acquired and congenital. III. The effects of abnormal arteriovenous communications on the heart, blood vessels and other structures. *Arch Surg* 11 (1925) 25
- SCHERF C. DALCHERTY G. GRIZZARD L. and IRELLY J. Arteriovenous fistula of the kidney. New observations and report of three cases. *Circulation* 19 (1959) 667

UROGRAPHY WITH UREA WASH-OUT IN RENOVASCULAR HYPERTENSION

A comparison with split renal function tests and predictive value

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M. C. PLAINTORRE, M. LAVAL JEANTET, J. BERNARD
and P. MILLIEZ

The split renal function and plasma renin activity determination in the renal veins in hypertension are generally considered two of the more reliable examinations to decide whether a renal artery stenosis is significant and therefore likely to benefit from surgery (FOSTER et coll 1969, FOURNIER et coll 1971, MAXWELL et coll 1968, SHAPIRO et coll 1969, STAMEY 1965). GUIDON et coll (1972) and the present authors (FOURNIER 1971) believe that the former test has a higher predictive value than the determination of the plasma renin activity in the renal veins if the criterion for ischaemia (FOURNIER et coll 1971, FOURNIER 1971) be based only upon the increased urinary concentration of creatinine (dU Cr). The former moreover requires painful instrumentation and is not without hazards (SAFAR et coll 1970, SHAPIRO et coll 1969).

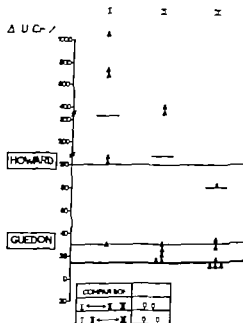


Fig 2 Late concentration of contrast medium in pelvis before and after urea wash-out and urinary concentration of creatinine ($\Delta U Cr \%$) I = present at 15 min (20 cases) II = revealed with wash out (12 cases) III = negative wash out (19 cases)

sodium and creatinine were measured only when the total urinary output was > 3 ml/min indicated by three minute collections

Separate measurements of inulin and PAH clearances were performed also in 35 and 32 cases, respectively. The PAH and inulin were infused with a constant rate pump after the injection of the priming dose. The three urine collections were begun 45 minutes after the start

The percentage disparity between the two kidneys was calculated for each determination. The difference between the kidneys was divided by the value of the normal or less diseased side and then multiplied by 100. When the stenosis was bilateral the kidney with the lower U Cr was selected. It must be pointed out that this differs from the method of HOWARD et coll (1964) in which the $\Delta U Cr$ is calculated by dividing the difference between the two sides by the value of the diseased side so that its 50 per cent in $\Delta U Cr$ equals a 100 per cent increase in our calculation

Results

Correlation between the urographic signs and split renal function

Correlation between a delayed appearance time and disparity in the separated clearance of inulin ($\Delta C I_n \%$) Figure 1 reveals that the mean decrease of C In on the diseased side is lower (— 32 per cent) for the group with the delayed

Tabl 1
Predictive value of urographic signs

Urographic sign	Sign present		Sign absent		χ^2 (p)	Cor- rectly clas- sified (per cent)	False positive (per cent)	False negative (per cent)
	Im- proved	Unim- proved	Im- proved	Unim- proved				
Size decrease ≥ 1 cm	25	8	18	2	NS	51	15	31
Delayed appearance time	29	1	14	9	< 0.005	73	2	23
Increased concentra- tion of contrast medium in pelvis 15 mm film	28	2	15	8	$= 0.023$	63	4	31
Positive urea wash out test	38	3	5	7	< 0.0005	84	6	10
Delayed appearance time and positive wash out	23	1	20	9	< 0.05	60	3	37

appearance time than for that without the sign (— 15 per cent) although this difference is not significant (Wilcoxon test)

Correlation of increased concentration of contrast medium in the pelvis with difference in the urinary creatinine concentration (Δ U Cr %). Figure 2 indicates the values of Δ U Cr per cent for the 50 cases in which urine separation was performed. These cases were divided into the following groups: group I with increased concentration of contrast medium in the pelvis in the 15 mm film; group II with the concentration only after urea perfusion; and group III without concentration even after urea perfusion. The Wilcoxon test discloses that the Δ U Cr percentage is significantly greater in group I than in groups II and III taken together as well as in group I plus II than in group III. It has been pointed out that in the 30 cases without pelvic concentration in the 15 mm film the urea wash-out revealed an increase in 12 cases which had a Δ U Cr greater than 15 per cent. However in one case (indicated by X in the figure) the increase disappeared after the urea infusion. Increased concentration was evident in the 15 mm film in only one case whereas the Δ U Cr was 9 per cent; such increased concentration was, however, associated with a larger collecting system.

Table 2

Value of urography in the diagnosis of curable renal vascular hypertension (43 cases)

		No. of cases	Incidence (per cent)
A			
Incidence of the various signs	Size decrease ≥ 1 cm	25	58
	Delayed appearance time	29	67
	Increased concentration of contrast medium in pelvis 15 min film	28	65
	Positive urea wash-out	38	88
B			
Incidence of normal urography according to the technique	Standard	10	23
	Standard + rapid sequence films	4	23
	Standard + rapid sequence films + urea wash-out	1	2.3
C			
Incidence of signs combination	Size decrease + delayed appearance time	23	53
	Size decrease + positive wash-out	23	53
	Delayed appearance time + positive wash-out	23	53
	The three signs combined	22	51

tween it and the urea wash-out test exists in 33 of the 35 cases. Only in 2 cases (indicated by X in the figure) was there contradiction since these 2 cases were improved by surgery whereas the urea wash-out was negative.

Value of urography in the diagnosis of curable renovascular hypertension

Part A in Table 2 indicates the incidence of the various urographic signs in the 43 cases in which hypertension was improved by surgery. The most frequent sign was a positive urea wash-out (88 per cent). Less frequent was the delayed appearance time (67 per cent), increased concentration of contrast medium in the pelvis in the 15 min film (65 per cent) or the decrease in size (58 per cent). The incidence of normal urography in curable renovascular hypertension depends on the technique (part B). This is 23 per cent with ordinary urography, 9 per cent when rapid sequence films are simultaneously available and 2 per cent when the urea wash-out test is added. The association of the various signs is presented in part C. The two signs occur in only 53 per cent of the cases and three signs agree in only 51 per cent.

Discussion

Correlation between the urographic signs and the split renal function

A delayed appearance time of the contrast medium is explained (MAXWELL & LUPU 1968) by the decrease in the glomerular filtration rate since these are excreted almost exclusively by glomerular filtration (FRY ET COLL 1967). The fact that no significant difference was observed in the ΔC In between the group in which the appearance time was later and the group in which it was symmetric does not mean that the above explanation is wrong. Indeed, other factors interfere in the assessment of a delayed appearance time, such as the superimposition of intestinal loops and technical defects, the difficulty in administering the contrast medium in less than 10 s and in obtaining accurate films each minute during the first 5 minutes.

A significant correlation was observed between the increase in the concentration of the pelvic contrast medium before or after the urea wash out and ΔU Cr. The overlap between the groups is however great and in 9 cases with negative wash-outs the ΔU Cr was between 15 and 94 per cent. These data indicate that a negative urea wash-out cannot eliminate renal artery stenosis of functional origin. On the other hand, a positive wash-out on the side of the stenosis with no obvious urologic explanation for this result is practically pathognomonic except in one instance (with urologic stasis) all cases with a positive wash out were associated with an increase of 15 per cent or more in the ΔU Cr i.e. the highest functional disparity observed in essential hypertension without renal insufficiency by GUZDOW ET COLL.

These facts lead to the practical conclusion that the split renal function test is unnecessary when the urea test is positive on the side of the renal artery stenosis (without obvious urologic factors) but is still necessary when the latter is negative.

Comparison of the predictive value of urography and split renal function test

The assessment of the predictive value of the various urographic signs indicates that the urea wash-out had the highest value with 84 per cent correctly classified cases. Since disparity in size has no predictive value it is important in assessment of the predictive value of urography to consider each sign individually and not to label the urography as either normal or abnormal. The latter method of assessment was used by AMSTEDDAM ET COLL (1969) and it is not surprising that they failed to arrive at any predictive value for urography.

The authors in a previous article (FOURNIER ET COLL) have argued that the classic criteria for the rechaemia of HOWARD ET COLL and GUZDOW ET COLL may exclude numerous cases that might benefit from surgery. One of the reasons for

the absence of sensitivity in these criteria was the simultaneous requirement of decrease in the urine flow and urine concentration of sodium. The present data confirm the predictive value of urinary creatinine concentration but not with the threshold of 100 per cent suggested by HOWARD *et coll*. The best prognostic classification is achieved here with the threshold of 15 per cent. The choice of this threshold would appear relevant since GUZDOV *et coll* have indicated that in essential hypertension without renal insufficiency functional disparity never exceeded 15 per cent. This criterion when applied to the present series led to only one false negative case in which the lesion was an aneurysm associated with marked renal parenchymal fibrosis.

A comparison of the urea wash-out and the $\Delta U Cr$ as regards their predictive values indicated fairly good agreement except in 2 cases which confirmed the lower sensitivity of the former.

Value of urography in the diagnosis of curable renovascular hypertension

This value is high if all the technical potentialities be employed, i.e. the rapid sequence films and the urea wash out. If the presence of only one sign in a urography be required to select cases for angiography, only 2.3 per cent of cases of curable renovascular hypertension will be overlooked. Since this percentage is not negligible, angiography is still indicated even with a normal urography when severe hypertension has suddenly occurred in a young subject, when an abdominal murmur is present, or when hypertension is recorded after lumbar pain or lumbar trauma.

Conclusions

A comparison of urography and the split renal function examination was made in 50 cases of renal artery hypertensive lesions. A decrease in the inulin clearance on the diseased side was unassociated significantly with the delayed appearance time of the contrast medium. An increase in the urinary concentration of creatinine ($\Delta U Cr$) was associated significantly with increased concentration of contrast medium within the pelvis before ($p < 0.01$) and especially after a urea wash-out ($p < 0.001$). Nine out of 19 cases with a negative wash-out had however a $\Delta U Cr \geq 15$ per cent which is the highest disparity between the two kidneys in essential hypertension. The increased pelvic concentration was always associated with a $\Delta U Cr \geq 15$ per cent except in one case with urologic stasis.

The predictive value of the urographic signs was assessed in 53 cases subjected to surgery. The sign with the highest prognostic value was the urea wash-out test with 84 per cent correctly classified cases, 6 per cent false positive and 10 per cent false negative.

The predictive value of the ΔU Cr alone was confirmed. The threshold value of 15 per cent gives the best prognostic classification. A comparison of the predictive value of this latter criterion with the urea wash-out presented good agreement except in 2 cases in which the hypertension improved after surgery and in which the ΔU Cr was ≥ 15 per cent but for which the urea wash-out was negative.

These data lead to the practical conclusion that the split renal function examination, nearly always painful, is necessary only when the urea wash-out is negative.

SUMMARY

Sixty-eight cases of renal artery stenosis revealed by nephroangiography were investigated with serial urography with a urea wash-out and a split function examination. A positive urea wash-out appeared to be the best urographic sign of unilateral renal ischaemia although negatives occurred. Its practical value lay in both the screening of renovascular hypertension and in indicating the results of surgery. This result leads to limit the indications of split renal function examination to stenosis with negative or dubious urea wash-out test.

ZUSAMMENFASSUNG

Achtundsechzig durch Nephroangiographie nachgewiesenen Fälle von Stenose der Nierenarterien wurden durch Serienurographie mit einer Durchspülungsurographie und einer separaten Funktionsprüfung der Nieren untersucht. Eine positive Durchspülung schien das beste urographische Zeichen einer unilateralen Nierenischämie zu sein, obwohl negative Befunde vorhanden waren. Der praktische Wert dieses Verfahrens liegt sowohl in der Massenerkennung von Fällen mit renovaskulärer Hypertonie als auch in einem Indikator für chirurgische Ergebnisse. Das Ergebnis führt dazu, dass eine separate Nierenfunktionsprobe nur in den Stenosen mit negativem oder zweifelhaftem Wash-out indiziert sei.

RÉSUMÉ

Les auteurs ont examiné par urographie en série avec lavage à l'urée et séparation d'urée 68 cas de sténose de l'artère rénale révélés par néphroangiographie. Le wash-out à l'urée pouvait paraître être le meilleur signe urographique d'ischémie rénale unilatérale bien qu'il y ait eu des cas négatifs. Sa valeur pratique réside à la fois dans le dépistage de l'hypertension rénovasculaire et dans l'appréciation des résultats de la chirurgie. Ce résultat conduit à limiter les indications de l'exploration fonctionnelle rénale aux sténoses dont l'épreuve du lavage à l'urée est négative ou douteuse.

REFERENCES

- AMPLATZ R. Two radiographic tests for assessment of renovascular hypertension. A preliminary report. *Radiology* 79 (1962) 807.
 AMSTERDAM E. A. COUCH M. P. COBBLESLIE A. R. et coll. Renal and renal activity in the prognosis of surgery for renovascular hypertension. *Amer J Med* 47 (1969) 861.

- FORSTER J H, RHAMY R H and OATES J A. Renovascular hypertension secondary to atherosclerosis. *Amer J Med* 46 (1969) 750
- FOURNIER A. Hypertension rénovasculaire. I. Comparaison des différentes investigations de dépistage. II. Comparaison des différentes investigations permettant de prévoir l'effet de la chirurgie sur l'hypertension artérielle. *Presse méd* 79 (1971) 903
- , ROSENBERG J M, SALMON D, MEYER P and MILLIEZ P. Predictive criteria of surgical curability of renovascular hypertension. Comparative assessment individually and in combination by discriminant analysis. *Acta med scand* 189 (1971) 391
- , SAFAR M, VIEILLON B, PAPAIOPOULOU N et MILLIEZ P. L'exploration fonctionnelle rénale séparée dans l'hypertension rénovasculaire. Détermination du meilleur critère pronostique. *Path Biol* 19 (1971) 71
- FRY I K, CATTILL W R, SPENCER A G and PURKIS P. Excretion urography. II. The relation between excretion and the intravenous urogram. *Brit J Radiol* 40 (1967) 572
- GUEDON J, BOURTBOURNIEUX A et LOURVET P. L'étude hémodynamique rénale séparée dans l'hypertension artérielle. Valeur diagnostique et pronostique à partir de 52 observations. *Presse méd* 73 (1963) 247
- , SAFAR M, FOURNIER A, MEYER P et MILLIEZ P. Prognostic value of simultaneous renal excretion renal and split function studies in unilateral renal hypertension. *Europ J clin Biol Res* 17 (1972) 757
- HOWARD J E, CONNOR T B and THOMAS W C. Use of differential renal function studies in diagnosis of renovascular hypertension. *Amer J Surg* 107 (1964) 58
- LEFFRANCE J, SAUTIEL J et BARGELLO R. Valeur de l'urographie endoveineuse avec épreuve de diurèse osmotique (wash out) dans le diagnostic et l'évaluation de l'hypertension rénovasculaire. *Ann Radiol* 11 (1968) 127
- LEVITT J I, AMPLATZ H and LOREN M K. Renovascular hypertension. *Radiology* 91 (1968) 521
- MAXWELL M H and LUFU A. Excretory urogram in renal arterial hypertension. *J Urol* 100 (1968) 395
- et FRANKLIN S S. Étude des fonctions séparées des reins dans les sténoses artérielles rénales. In: *Actualités néphrologiques de l'Hôpital Necker*. Flammarion, Paris 1968
- REIDENBERG A H, SCHREIBER M H and SARTIN C H. The pyelogram urea wash-out test in the evaluation of renovascular hypertension. *Amer J Roentgenol* 107 (1969) 705
- SAFAR M, FIDLER J P, ECOFFIER J et MILLIEZ P. Valeur de l'exploration hémodynamique séparée et de l'activité rénale plasmatique pour la curabilité chirurgicale des hypertensiones rénovasculaires. *Presse méd* 78 (1970) 261
- SHAPIRO F, PEREZ STABLE E and SCHIEF E T et coll. Renal artery stenosis and hypertension. *Amer J Med* 47 (1969) 175
- SIMNEY T A. Renovascular hypertension. *Amer J Med* 38 (1965) 829
- STJERNAL R E, STA F W, LOREN M K and AMPLATZ H. The value of the urea wash-out test in the assessment of curable renovascular hypertension. *Amer J Roentgenol* 92 (1964) 1397
- WITTEN D M H et S C. SHIFFS S G et coll. Excretory urography in renovascular hypertension. Minute sequence filming and osmotic diuretic. *Amer J Roentgenol* 98 (1966) 114

PRINTING OF MULTICOLOR COMBINATION IMAGES INTENDED FOR ROENTGENOLOGIC APPLICATION

H J PARHMAN and U WELANDER

Roentgen images may after conventional processing, be treated in different ways by electronic or photographic methods. Such procedures may yield information only obtained with difficulty, if at all, on direct inspection of the original films.

A method by which color processing may be used for demonstrating the movements of the contrast medium at angiography has been presented by WELANDER (1969). This technique, which produces a multicolor combination image composed of several phases from a serial angiography, permits a larger anatomic segment of the blood vessels to be investigated at one and the same time than is possible in the individual component views. Variations in hue caused by differences in the distribution of the contrast medium between the component views are also depicted in the combination image. As these differences are related to the flow rate through different vessel details concerning the circulation may also be examined in one single image (Fig. 1).

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Starting with three different black and white films a multicolor combination image is prepared by first converting the three originals into three different colors (Fig 2). These three monochromatic color images are then combined to form a multicolor image in which all details in the original views are seen simultaneously. A detail which is present in only one of the three component views will appear in the combination image in the color belonging to that view. Details which are present in two component views or in all three appear in compound colors. If the three subtractive primary colors yellow, magenta and blue green (cyan) are used, the details appearing in the yellow and the magenta views will be red and those in the magenta and the cyan views will be blue; the details present in all component views will be gray or black when the density is the same in all the original films and when this is not so they appear in various brownish hues. It is thus possible to determine from the combination image which details were present primarily in the respective original images: details in yellow, red and green were present in the first component view, those in magenta, red and blue in the second view, and those in cyan, green and blue in the third view, while details in gray, black and brownish hues were present in all component views. Such color shifts in combination images provide information of diagnostic value (LILJEQUIST & WELANDER 1969, WELANDER 1969, LILJEQUIST & WELANDER 1970).

Several difficulties are encountered when multicolor combination images are to be printed for publication and the present paper will attempt to describe the method used in the production of the illustrations in WELANDER's original thesis. This method may be applied in all cases with analogous prerequisite conditions.

Reproduction of color films. A printed color image is usually produced by the four color printing method. Yellow, magenta and cyan dyes are used to create the color image and black dye to intensify the saturation of the colors in areas in shadow or relief as well as in black or gray details.

There are an infinite number of spectrum colors, but they may all be represented by mixing so-called primary colors: either the additive primary colors blue, green and red or the subtractive primaries, yellow, magenta and cyan. All the color sensations experienced in everyday life may be produced by combining in different ways the hues in these two groups of three colors. Color reproduction is based on this three color principle.

Starting from a multicolor original film, color separation is first carried out and the original reproduced photographically or electronically through different filters. Light corresponding to the blue violet part of the spectrum is transmitted through a blue violet filter and yellow light is absorbed; a green filter lets through the green part of the spectrum and absorbs red; and an orange red filter



Fig 1 Congenital arteriovenous malformation. The multicolor combination image (d) gives a comprehensive view of the abnormality. The color shifts in the blood vessels are caused by differences in the distribution of the contrast medium in the different component views (a, b, c) and are thus a reflection of the circulation.



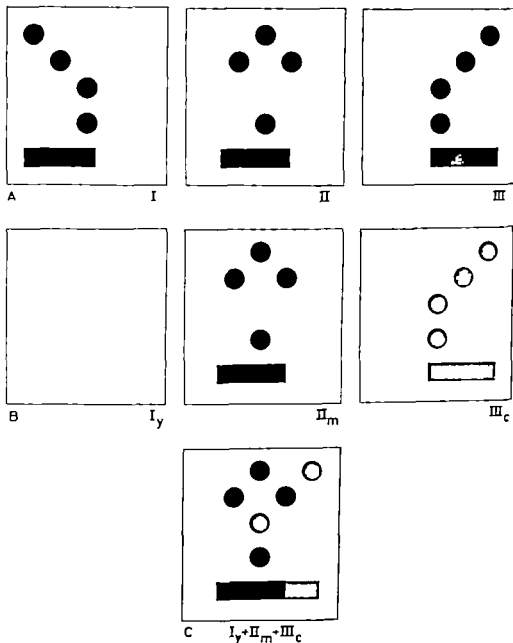


Fig. 2 Schematic representation of the construction of the combination image. Three different views (A I, II and III) are converted into monochromatic color images (B I_y , II_m and III_c) and when these are combined the multicolor combination image (C) is produced. When viewed in the opposite direction (pwards) the figure illustrates the division of multicolor image into monochromatic component images—a color separation.

transmits the yellow red part and absorbs blue. The printing plate for yellow is prepared with the aid of a blue violet filter, the plate for magenta with a green filter, and that for cyan with an orange red filter. Thus, the negatives obtained through the color separation represent the filter colors while the positive image that is to be printed is represented by the absorbed colors. A yellow filter is used as a rule in the preparation of the black plate, but this may be varied, depending on the color nature of the film.

In connection with the color separation, the image is screened through a dot or linear screen. When printing plates for color printing are being prepared, the screen used for the reproduction must be rotated a certain number of degrees between each color in order to avoid the formation of disturbing moiré patterns or to prevent the dots from exactly overlying one another during the printing and thus neutralizing the individual color effects. Great care must be taken when printing to obtain correct registration of the monochromatic color images.

The additive primary colors, blue, green, and red, will appear when the component views are combined in pairs: those details that are printed in both magenta and cyan will be blue; those printed in yellow and cyan will be green; and those in yellow and magenta will be red. Gray and black appear when the same amount of subtractive primaries is present in all three of the colored component views, but in four color printing they are strengthened with the aid of a black and white image.

The principle underlying the reproduction of color images is illustrated in Fig. 2. Starting from the multicolor image (Fig. 2c), color separation is carried out (Fig. 2b), and printing plates are then prepared from these images (Fig. 2a). When the three images are printed together, the original color image is re-created. The three color process has been used in this particular example, and the supplementary black and white image has been left out since the latter is of no significance to the colors in the final product.

Multicolor combination images. The conventional procedure for the preparation of printed images as described causes problems when applied to multicolor combination images. It is complicated, time consuming, and consequently also expensive. The transmission of different wave length ranges through the color filters at present available for color separation is not so perfect that the component images obtained through the separation agree in all details with the original images.

In connection with the presentation of WELANDER's technique for producing multicolor combination images, it was desirable to produce illustrations in which there was total agreement between the reproductions of the black and white originals and the multicolor combination images. In order to solve this problem,

the reproductions of the multicolor combination images were made directly from the black and white originals. These original films may in fact be regarded as perfect color separations of the combination images. It is thus possible to produce multicolor combination images in print without applying the process of color separation.

The new method. The black and white originals were provided with register marks in order to ensure perfect adjustment when the images were superimposed and the plates were then made directly from these originals. A Vario-Hilso-graph was used as the engraving machine.

The original, either a reflection copy or a transparency, is placed in the optical part of the machine and is scanned by a light source from a small aperture. The scanning head moves sideways between each scanning line so that the whole original is scanned and a linear screening thus arises in connection with the scanning. The length of the lateral movement is determined by the degree of enlargement or reduction desired and by the screen ruling selected as suitable for the printing paper. Simultaneously with the scanning impulses are fed to the engraving head of the machine which makes a corresponding cut in the plate inserted in the engraving system. The original image contains density variations that may range from pure white to pure black. The scanning system reacts to these densities and sends signals to the engraving system so that its engraving stylus cuts down into the plate to a depth corresponding to the density of the original. The stylus makes a deeper cut in those parts that correspond to the areas of low density in the original, and thus leaves only a small space between the screen lines—a small printing dot. For areas of high density the conditions are reversed and larger printing dots are produced. The machine contains units allowing electronic control of the contrast and density range of the image as well as control of outline sharpness and is also equipped with a sensitive unit for measuring the density of the original.

The plate making work results in three plates, one from each black and white component of a multicolor combination image. In principle, the plates are equivalent to conventional black and white plates but outline sharpness and gradation are controlled electronically and the screen angle is varied 30° between screen positions (15°, 45° and 75°) in order to avoid the moiré effect mentioned earlier.

The plates, after completion, may be used in the printing of reproductions of the original component views in black and white (Fig. 1 a, b, c). If they are superimposed in color—in yellow, magenta and cyan—a multicolor combination image (Fig. 1 d) true in every detail to the black and white reproductions of the originals, will be obtained.

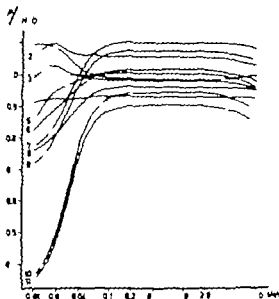
Discussion

The method for the preparation of printed multicolor combination images now presented is in reality analogous to photographic or electronic methods: it is a graphic procedure for producing combination images.

Its advantages are obvious. The reproduction is carried out in one step: directly from the original to the plate, and without a camera, reproduction negatives or copying. Furthermore, apart from the advantage that outline sharpness and gradation can be regulated, it is also of value that the possible sources of error and uncertainty factors always involved in work requiring several steps are eliminated. Another important advantage is the exact agreement that can be achieved between individual details in the reproductions of the black and white originals and of the multicolor combination image: this will be perfect if the same plates are used both for the color printing and for the black and white prints, so that direct comparisons may be made between the originals and the multicolor combination image. It is not necessary to use the same plates in order to achieve this result; however, two identically similar plates, one for each black and white image and one for each monochromatic component image, may be prepared in accordance with the method described. If, on the other hand, conventional methods are used for preparing the images, it is not possible to guarantee that the reproductions will be correct and alike in all details: there may be a risk of the illustrations being misleading.

This color printing method is applicable when a photographically or electronically produced color image is composed of separate originals that may be regarded as color separations. A considerable simplification is achieved in such cases, while at the same time the information in the originals is portrayed more correctly than with other techniques. As far as the writers can judge from the reproductions of color images published hitherto, this simplified method has not been used by others, even when the same fundamental prerequisites have been present in the basic material.

The engraving machine used for the plate making is in reality intended for the preparation of color reproductions and it is therefore equipped with a complicated combination of a filter system and a system for electronic color correction for color separations. However, it also permits electronic regulation of outline sharpness and gradation and contains excellent possibilities for measuring the density of the originals. It may therefore also be used to advantage for the reproduction of black and white originals in which the requirements with respect to sharpness of detail and small differences in density are particularly high, as with roentgen films.



Linear attenuation coefficients in relation to water: 1 — Mixture 1, 2 — M 3, 3 — Silica paraffin wax, 4 — Mixture 2, 5 — M 5, 6 — Siemens wax, 7 — Methylmethacrylate, 8 — Pressed wood, 9 — Polyethyleneglycol A 1000, 10 — Paraffin wax ($\mu_0 = 0.02$), 11 — Paraffin wax ($\mu_0 = 0.88$).

In order to estimate the attenuation properties of a composite material the concept effective atomic number was introduced (WALTER 1927, MAYNEORD 1937). Its definition varies (SPIZER 1946, MARKUS 1956, EVANS 1964, WEBER & VAN DEN BERG 1967) demonstrated that the common formulas for effective atomic number are not applicable when both coherent and Compton scattering is of importance. Another drawback of the concept is that it does not allow a quantitative estimate of the importance of a difference in effective atomic number between the phantom material and soft tissue. Also the relative importance of the effective atomic number and electron density varies with photon energy.

It is a fairly simple matter to calculate the linear attenuation coefficient at different photon energies for any material of given chemical composition and mass density. Such a description should therefore probably be preferred.

Material Method and Results

The linear attenuation coefficients for various phantom material in relation to water were calculated for monoenergetic photons in the interval 10 keV to 10 MeV. The chemical composition of the materials were taken from HEMMINGSSON (1971) and the attenuation coefficients from ATTIA & ROSEN (1968). The calculations were done on a Siemens 305 computer. The results are presented in the figure.

Discussion

The figure discloses that for photon energies above 40 keV Mixture 1 Silica paraffin wax, Mix D and Siemens wax are good substitutes for soft tissue while the attenuation in the other materials differs appreciably from that in water. For photon energies below 40 keV only silica paraffin wax appears to offer a good substitute. These statements cannot be readily made from the mass densities, the electron densities and the effective atomic numbers of the materials (cf. HENNINGSSON 1971).

Acknowledgement

Computer time was generously granted by Elekta Schonander AB Solna, Sweden.

SUMMARY

The linear attenuation of photons between 10 keV and 10 MeV in various phantom materials relative to water was calculated and the validity of the effective atomic number discussed.

ZUSAMMENFASSUNG

Die lineare Absorption von Photonen zwischen 10 keV und 10 MeV in verschiedenen Phantommaterialien relativ zum Wasser wurde berechnet und die Gültigkeit der effektiven Atomnummer diskutiert.

RÉSUMÉ

Les auteurs ont calculé l'atténuation linéaire de photons entre 10 keV et 10 MeV par rapport à l'eau dans des fantômes faits de différents matériaux et ils examinent la validité du numéro atomique effectif de ces matériaux.

REFERENCES

- ATTIX F H and ROESCH W C. Radiation dosimetry. Second edition. Vol 1. Academic Press, New York and London 1968.
- EVANS R D. X-ray and γ -ray interactions. I. Radiation dosimetry. Second edition. Vol 1. p. 93. Edited by F H Attix and W C Roach. Academic Press, New York and London 1968.
- HENNINGSSON A. Cervical phantom for evaluation of different methods of oxygen estimation of the larynx. Acta radiol. Diagnostica 11 (1971) 515.
- JAYARAMAN C V. Calculated effective atomic number and kerma ratios for tissue equivalent and dosimetry materials. Phys. in Med Biol. 16 (1971) 617.

- MARALIS B. Über den Begriff der Gewebeäquivalenz und einige wasserähnliche Phantomsubstanzen für Quanten von 10 keV bis 100 MeV sowie schnelle Elektronen. Strahlen therapie 101 (1956) 111
- MAYNEORD W. V. The significance of the roentgen. *Acta Un. int. Cancr.* 2 (1937) 271
- SPRUELL F. W. Materials for depth dose measurement. *Brit. J. Radiol.* 16 (1943) 90
- Effective atomic number and energy absorption in tissues. *Brit. J. Radiol.* 19 (1946) 59
- WALTER B. Über die besten Formeln zur Berechnung der Absorption der Röntgenstrahlen in einem beliebigen Stoff. *Fortschr. Röntgenstr.* 35 (1927) 929
- WEBER J. and VAN DEN BERG D. J. The effective atomic number and the calculation of the composition of phantom materials. *Brit. J. Radiol.* 42 (1969) 378

DESCRIPTION OF A FILM CHANGER FOR SMALL ANIMALS

L. G. ANQANTYR and T. OLIN

Two different principles may be applied to obtain high definition serial angiography in small animals. The first is the use of direct roentgen magnification and the second the employment of industrial film in close contact with the animal with secondary photographic magnification. The direct magnification technique demands a fine focal spot capable of withstanding high tube loading so that the exposure time may be short. If the object film distance be kept small to minimize geometric blurring the second method may be performed with a simpler type of roentgen tube. A suitable film changer for small industrial films is not however commercially available so that the authors have developed an apparatus suitable for the purpose.

The apparatus consists of two units: the film changer itself and the programme selector. The changer is supported on four legs locked in position on rails at the side of a coordinate roentgen table. An overhead tube at a FFD of 45 cm is employed. The film plane is covered by a thin membrane of polyester and below

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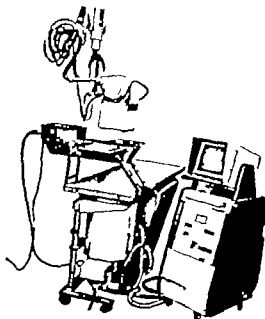


Fig 1 Film changer in position on a coordinate roentgen table. Fluoroscopy can be performed through the changer.

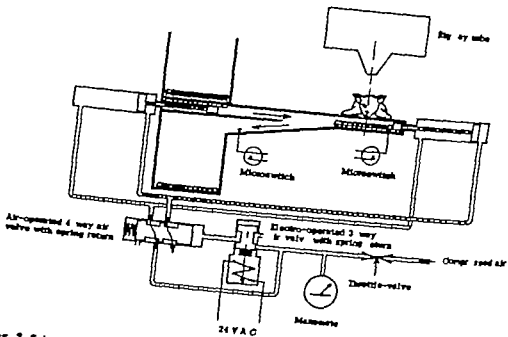


Fig 2 Schematic diagram of the film changer with magazines to the left. The pistons for film transport be on either side.

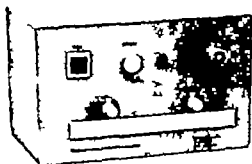


Fig 3 The programme selector the programme is set by the two lower control knobs

thus a space under the table houses an image intensifier and enables fluoroscopy to be performed with the animal in position on the changer (Fig 1) At one end of the film changer above the film plane a magazine holds the unexposed films 9 cm \times 12 cm industrial film, usually Agfa Gevaert Structurix D4 (Fig 2) A piston driven by compressed air (7 kp/cm²) moves the films into position for exposure and as soon as the exposure has been made a second piston ejects the films down into a collecting magazine situated below the one for the unexposed films These two magazines and the transport tunnel are shielded by 2 mm of lead The pistons that move the films are maneuvered by a four way valve operated with compressed air through an electromagnetic valve A microswitch in the film changer closes the roentgen circuit as soon as the film is in position The films are attached to one side of thin plexiglass sheets 11 cm \times 16 cm before being loaded so that the transport of the film is stabilized and made reliable the magazine holds up to 12 films

The programme selector contains the control unit for roentgen exposures and film transport (Fig 3) The apparatus is connected to the mains by a transformer stepping down the voltage to 24 V to supply the transistor circuits that constitute the brain of the apparatus (Fig 4) A delay relay insures that the rotation of the anode of the roentgen tube has reached maximum speed before the film changer operates An electronic oscillator generates a basic frequency of 1 Hertz which runs the changer via two counters Two sequences may be chosen on the selector The first is run at 1 film/second for 1 to 9 seconds When the sequence is completed the next continues with a time interval between the films of 1 2 4 or 8 seconds until the magazine is empty and all the films have been exposed the film changer will then stop automatically

Two switches in the changer prepare the programme selector when the film is in position for exposure and after it has been transported away so that the next film can be moved into position guided by these two signals the programme

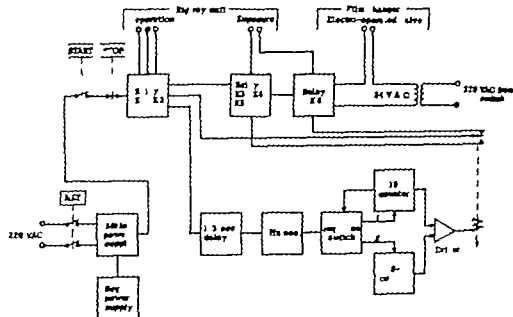


Fig. 4. General plan of the film changer.

selector manoeuvres the electromagnetic high pressure valve that controls the film transport.

The film changer in practice is operated in the following manner. The film magazine is loaded and the roentgen generator is connected to the film changer by pressure on a button on the roentgen control panel. The film changer is then started by pressing the start knob on the programme selector panel. The anode will begin to rotate and the two control panel lights on the programme selector will indicate that the apparatus is ready. As soon as the knob is released the film changer will commence to operate and will run through the selected programme until all the films of the programme selected have been exposed. The rotation of the anode is terminated by pressing the stop knob on the selector. Finally the collecting magazine is emptied and the films developed.

The film changer has been in regular use for a year, particularly for the angiographic examinations of rats, but it has also been employed in rabbits and cats. The apparatus has been found to be reliable and without defects. The quality of the films has been somewhat higher than direct fourfold magnification with a $0.1 \text{ mm} \times 0.1 \text{ mm}$ focus tube and an ordinary film changer (AOT 24 cm \times 30 cm Elema Schönander Sweden) with high definition screens. The unit could be further developed. If the transport paths for the films were shortened it would be possible to increase the speed to 2 films/second; the size of the films might also be increased — say to 13 cm \times 18 cm.

SUMMARY

A film changer fitted to a roentgen table for examining small animals is described. The design permits the performance of high definition serial radiography.

ZUSAMMENFASSUNG

Für die Untersuchung von kleinen Tieren wurde ein Filmkassettenwechsler konstruiert und am Röntgentisch befestigt. Diese Apparatur erlaubt die Anfertigung von scharfen angiographischen Bildern.

RÉSUMÉ

Description d'un changeur de films adapté à une table radiographique pour l'examen de petits animaux. Ce dispositif permet l'exécution de radiographies en série de haute définition.

TOMOGRAPHY OF MOVING OBJECTS

SVEN REICHMANN

Tomography is usually dependent on three components: the focus, the film and the object, the tomographic effect being obtained by moving two of these components with the third stationary. Special problems arise when the object itself is moving, as in and around large blood vessels, the pulmonary hilum and the common bile duct are good examples. The traditional technique in pulmonary tomography implies linear movement, the usual reason for the choice of which is a short exposure time. However, most tomographs still need several tenths of a second to perform linear movement and BLOEDNER (1964) argued that even during such an exposure considerable movement of the pulmonary vessels must occur. He therefore recommended elliptical tomography with an exposure time of several seconds; he compared linear and elliptical movements by means of simultaneous multisection tomography and was unable to find linear movement superior in spite of its exposure time.

WESTRA (1966) commented upon the technique in tomography and zonography of the common bile duct. He was of the opinion that movement of the duct gave rise to poor definition in zonograms produced with a circular movement and accordingly recommended a larger tomographic angle in compensation. He argued that movement unsharpness made the common bile duct



Fig. 1 Pulmonary hilum tomographed in the same plane with hypocycloid (a) and transversal linear movement (b). The degree of unsharpness is higher in (b). Arrows in (b) indicate spurious contours from motionless structures outside the tomographic plane.

equally unsharp as lightly blurred image components in zonography and an increase in tomographic angle were employed to increase the difference in blurring between the bile duct and masking structures.

When the object to be tomographed is moving it is surprising that an acceptable tomogram can be obtained at all. Since it was apparent (Fig. 1) that a difference in image unsharpness occurs when for example hypocycloid movement with its exposure time of six seconds is replaced by linear movement with an exposure time of 0.75 seconds, it was considered important to determine how a tomogram is formed when the object is moving.

Theoretic analysis

The movement of the objects is usually of an accelerating or decelerating nature as movements of constant velocity are rarely encountered in the living body. The tomographic depiction of objects moving at constant velocity must however be analysed before the effects of acceleration and deceleration are taken into account.

Tomographic representation of an object moving at constant velocity appears in figure 2. For the sake of simplicity a linear tomographic movement is used, the focus travelling from A to B during the exposure with a point within the moving object being situated at A_1 at the beginning of the exposure. During the exposure this object point moves so that it lies at B_1 when the exposure ceases. It will be realized from the figure that the object point in question may

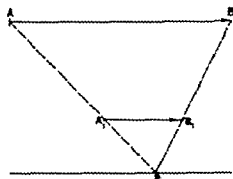


Fig. 2 Tomography of object moving at constant velocity. A point within the object moves from A to B when the focus moves from A to B. The projection is constant onto point P. Sharp definition is obtained if the tomographic plane passes through this point.

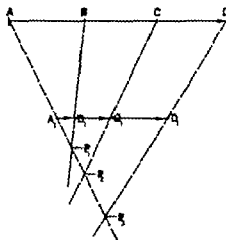


Fig. 3 Tomography of accelerating object with conditions identical with those of Fig. 2. The object point is not depicted in one single tomographic plane as in Fig. 2, but the image descends as indicated by points P_1 , P_2 , and P_3 ; thus no tomogram can arise.

be projected onto one constant point, called P in figure 2. If the tomograph be adjusted so that its tomographic plane passes through this point P the moving object point will have projected without movement onto the film during the whole tomographic exposure since every point in the tomographic plane has a constant projection. Thus, the movement of the object makes it possible to obtain a representation of an object part outside the tomographic plane. When the object moves in the same direction as the focus, sharp depiction is obtained from any object parts above the tomographic plane. In the same way if the movement be the opposite, structures below the tomographic plane will be sharply presented. It will also be evident from figure 2 that the greater the velocity of the object, the greater will be the distance from the tomographic plane for object components sharply outlined in the final tomogram.

The effect of acceleration appears in figure 3. The focus travels at constant speed along path ABCD. When the focus moves from A to B the object point moves from A_1 to B_1 and when from B to C the object point moves from B_1 to C_1 and so on. Since the movement is accelerating the object point travels successively longer distances when later parts of the exposure are compared with earlier ones. The central roentgen ray from the focus positions A, B, C and D coincides at points P_1 , P, and P_2 instead of at one single point. There is thus no tomographic plane where sharp depiction may be obtained. It may be

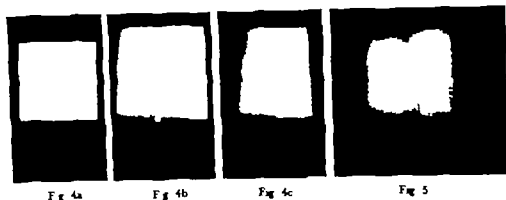


Fig 4a

Fig 4b

Fig 4c

Fig 5

Fig 4 Linear tomography (tomographic angle 10°) of metal cylinder attached to metal rod so that pendulum movements may be performed. a) The tomographic plane passes through the cylinder which is motionless. The tomograms of the moving cylinder have been taken from the same series of multisection tomograms. b) The tomographic plane passes through the cylinder and c) far outside it the contours are still sharp.

Fig 5 Linear tomography (tomographic angle 40°) of the same moving cylinder as in Fig 4. The tomographic plane is outside the cylinder as in Fig 4. Owing to the long exposure time the pendulum has changed its direction of movement several times and led to the appearance of several cylinder images since the tomographic plane is outside the cylinder these different images are only partially superimposed.

concluded that under the conditions prevailing in figure 3 no sharp representation can occur in tomography of an accelerating object. Likewise it may be demonstrated that deceleration also makes this impossible.

The general conclusion is that object movement in itself does not necessarily preclude sharp tomographic representation in linear tomography even when long exposure times are used. On the other hand a change in the velocity of the moving object may effectively prevent all sharp outlining. The same effect must arise if the object be moving at constant velocity and the tomographic movement be accelerating or decelerating.

Large blood vessels oscillate. The movements are limited by turning points where they change direction. When this change occurs no movement takes place for a short moment and between these extreme points one phase of acceleration and one of deceleration occurs. It may be expected that sharp tomographic representation is obtainable only when the movement is at one of its extreme points. Deviation may possibly also be expected in the middle of the movement when acceleration becomes deceleration. This hypothesis has been tested in a practical experiment.

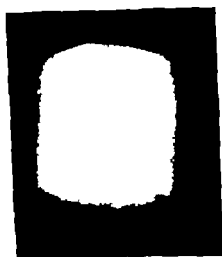
Practical test

The object to be tomographed was a small metal cylinder attached to the free end of a pendulum, the movement of which occurred in a plane parallel with the tomographic plane. Simultaneous multisection tomography by means of a Polytome was performed with seven films, the distance between adjacent films corresponding to a distance of 12 mm between the tomographic planes. The middle plane of the seven tomographic planes went through the cylinder the diameter of which was 24 mm: this diameter made it possible to obtain an accurate tomographic representation only in the middle tomographic plane when the cylinder was stationary. This was confirmed in a multisection tomogram obtained with a linear movement at right angles to the motionless cylinder surface the tomographic angle being 10°. This multisection tomogram also provided information about the amount of blurring in the different tomographic planes outside the cylinder when this angle was used.

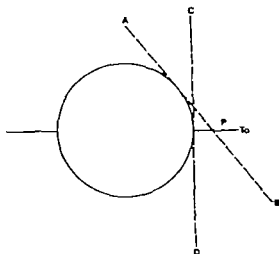
Linear and circular tomography was performed when the pendulum was moving. The linear movements were directed both along and at right angles to the main direction of the pendulum movement. Two tomographic angles were then used namely of 10° and 40°. The exposure time with the 10° angle was sufficiently short as to prevent the appearance of more than one turning point of the pendulum in the tomogram. When the angle was 40° several such turning points were registered. Circular tomography at an angle of 36° was also performed and a large number of turning points were registered in the tomogram.

A tomogram through the cylinder stationary appears in figure 4 a. The same plane obtained with 10° linear tomography and the movement parallel with that of the pendulum is represented in figure 4 b. A turning point then appears when the cylinder is situated as far to the left as possible and to the right of this image a zone of blurring formed when the cylinder was moving is evident. In figure 4 c the registration was made at the same time as that in figure 4 b although the tomographic plane was situated 36 mm away from that in the latter: the appearances are however similar. The stationary cylinder in the same tomographic plane was represented only by means of a blurred image: the movement of the cylinder thus produced the sharpness (Fig. 4 c). In principle the same type of result was obtained when the tomographic movement and the main direction of the pendulum movement crossed each other at right angles.

When the tomographic angle was increased from 10° to 40° in the linear movement a number of turning points occurred during the exposure. The resulting tomograms for this reason contain several images of the same cylinder. It was again evident that sharp definition could be obtained in tomo-



a



b

Fig. 6 Circular tomography (tomographic angle 36°) of the same moving cylinder as Figs. 4 and 5 with the tomographic plane passing through the cylinder. As explained (b) the images do not exactly coincide since different directions of the roentgen beam (AB, CD, etc.) will make the contours appear in different locations (P, P₂, etc.) in the tomographic plane. The multitude of contours lie close together since the tomographic plane passes through the cylinder. Their summation gives rise to image unsharpness in the tomogram (a).

graphic planes far outside the cylinder itself (Fig. 5). The different cylinder images were situated at a distance from each other so that they overlapped only partially. With a large tomographic angle the image contrast of each single contour was higher when the tomographic plane went through the cylinder than when the plane lay far outside the cylinder.

The theoretic analysis suggested that representation of the cylinder might be possible at the moment when acceleration turned into deceleration, the cylinder then moving at constant velocity. No registration of the cylinder attributable to this part of the pendulum movement path was however observed in any of the tomograms.

It may be concluded that an object that moves as a pendulum during a tomographic exposure is not blurred to the same extent as a stationary object. The best representation seems to occur in tomographic planes through the object and when the movement changes direction. The fact that sharp definition may occur in tomographic planes far outside the object is due to a sort of interference between the tomographic movement and that of the object. This occurred in the present test when the object was near the turning point of its movement path.



Fig. 7. Multisection linear tomography (exposure time 0.75 s) of a tumor in the posterior part of a pulmonary hilum. Propagated chest movements were evident at fluoroscopy. a) The tomographic plane passes through the tumour to give a low degree of unsharpness. b) The tomographic plane is 1 mm away from that in (a) which has rendered the contours more unsharp.

A tomogram from a tomographic plane through the cylinder when a circular movement was used with a tomographic angle of 36° appears in figure 6. The exposure time was long so that many turning points occurred during the exposure and were spread out by the large tomographic angle (fig. 6 b). Every contour in the final tomogram thus consisted of many partial contours that not exactly corresponded: this gave rise to a certain unsharpness of all contours. The conclusion from this experience is that all contours in a tomogram from a moving object are unsharp even when the tomographic plane passes through the object if the tomographic angle be large with the movement of the object turning many times during the tomographic exposure.

Clinical experience

The general conception that linear tomographic movement is preferable in pulmonary tomography owing to a shorter exposure time was supported by the phantom tests already described. When these tests had been performed it was realized that the exposure time should be sufficiently short that only one turning point of the object movement occurred during the exposure. Further shortening of the exposure time was regarded as useless. However, a new problem arose for the object movement was found to counteract the blurring of the motion.

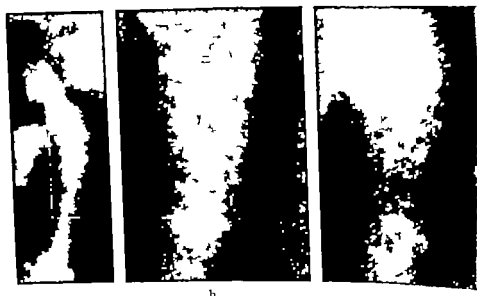


Fig. 8 Cholangiography (a) The common bile duct as indicated has the transverse linear movement (exposure time 0.3 s) and (b) a ureter (exposure time 3.0 s) at the same tomographic angle. Movement unsharpness in (c).

graphic movement. It thus proved necessary to test whether the movements in lung tomography is sufficiently effective. A tomography with seven films was used, the corresponding tomographs situated at 12 mm intervals. Nine subjects were examined with 70 kV performed with a linear movement and a tomograph with a Polytome. The exposure time was 0.75 s. When compared it was evident throughout that the tomographic effect counteracted to such a degree as to make this type of tomography. Hilar vessels that were sharply defined in one film were in the next film. A hilar tumour that moved with the vessels (Fig. 7) was likewise sharply defined in one plane but not in adjacent planes.

No systematic investigation of the technique of intravenous undertaken. Figure 8 presents a comparison between linear tomography (exposure time 3 s) and linear tomography (transverse linear movement exposure time 0.3 s) at a tomographic angle of 20°. There is a difference in unsharpness indicating that the linear movement is more effective.

This observation has been confirmed by clinical experience. Circular tomography (exposure time 3 s, tomographic angle 6°) was employed earlier but since a change to linear tomography (tomographic angle 20°) has been made the problems with image unsharpness have disappeared.

Discussion

The final image in tomography of a moving object arises through a kind of interference between the tomographic and object movements. This interference process under some circumstances may act in such a way that object parts far outside the actual tomographic plane may be sharply defined. On the other hand, those within the tomographic plane may be lost in the final image. When the object performs an oscillating movement the sharp contours of the tomogram arise when the movement changes direction and the object is stationary. An acceptably sharp tomogram may be obtained if the movement of the object changes only once during the tomographic exposure.

The movement of large blood vessels does not necessitate infinitely short exposure times. In fact very short times may be expected to produce high image unsharpness if the movement of the object cannot change direction once during the exposure. Acceptable unsharpness in pulmonary tomography was obtained in the present investigation with an exposure time of 0.75 s.

Interference between the two types of movement may give rise to a sharp representation of an object component situated far outside the tomographic plane. REICHMANN (1972a) has analysed the development of contours from object components far outside the tomographic plane in cases where no object movement occurs. Such contours were called *spurious contours* since they acquire their form not only from the shape of the object but also from the form of the tomographic movement path. When an object movement then occurs the contours seem to acquire their form only from the shape of the object with the one condition that the movement of the object be homogenous. Without the latter so that different parts of one single structure fail to change direction of movement at the same time the shape of the final contours will depend both on the form of the structure in question and its pattern of movement. It would thus appear that tomography of moving objects may produce a special kind of *spurious contour* owing to the movement of the object itself.

The risk of *spurious contours* being produced by this movement has been investigated in pulmonary tomography under certain specified conditions and proved negligible. The reason for this is obvious. The phantom tests revealed that a contour arising from an object component far outside the tomographic

plane will have a lower contrast than one from the same object when situated in the tomographic plane. The contrast of a pulmonary image is low and that of the spurious contours that derive from object movement will thus not be perceptible against the background of radiographic mottle. Precautions may however have to be taken when the contrast is high. This may occur when, e.g. calcifications are present in a lymph nodule of a pulmonary hilum.

Spurious contours with the same direction as the movement path of the focus usually occur in the final tomogram in linear tomography of motionless objects. The universal experience has been that this does not occur to the same degree in pulmonary as in skeletal tomography. One explanation (REICHMANN 1972 a) is that the differences in absorption are smaller in the lung than in the skeleton. However the present investigation has demonstrated that this is not the whole matter. The spurious contours of stationary objects usually develop when the focus travels along a boundary between two differently absorbing structures within the object, this boundary being situated far outside the tomographic plane. An important condition is that only if this process takes a considerable part of the total exposure time can spurious contours appear in the final tomogram (REICHMANN 1972 b). When the object is oscillating sharp contours can develop only when the direction of movement changes. This moment is such a small part of the total exposure time that the development of the spurious contours usually appearing in linear tomography of motionless objects is counteracted. The risk of this type of spurious contour emerging is not however eliminated in pulmonary tomography, some structures near the tomographic plane may be stationary and give rise to the phenomenon (Fig. 1 b).

The tomographs of today cannot perform multidirectional tomography of the lung or similar moving structures as one whole revolution at a satisfactory tomographic angle in less than a second is impossible. It would of course be interesting to construct a tomograph with such a rapid movement. The tomographic movement in multidirectional tomography is constantly accelerating perpendicular to its direction. As was pointed out in the theoretical analysis acceleration may be expected to reduce the risk of the occurrence of such spurious contours as arise from interference between the tomographic and object movements.

SUMMARY

A final tomogram of a moving object is produced from interference between the tomographic and the object movements. This process is analysed theoretically and practically. Certain important data on the length of the exposure time and on the type of tomographic movements are discussed.

ZUSAMMENFASSUNG

Ein endgultiges Tomogramm eines beweglichen Objekts wird aus der Interferenz zwischen den tomographischen und den Objekt-Bewegungen hergestellt. Dieser Vorgang wird theoretisch und praktisch analysiert. Gewisse wesentliche Daten über die Länge der Expositionzeit und der Art der tomographischen Bewegung werden besprochen.

RÉSUMÉ

Le resultat final de la tomographie d'un objet en mouvement resulte de l'interference entre le mouvement tomographique et le mouvement de l'objet. Ce processus est analyse theoriquement. L'auteur examine certaines donnees importantes concernant la longueur du temps d'exposition et le type de mouvement tomographique.

REFERENCES

- BLOEDERER C. D. Schichtuntersuchung der Lunge mit mehrdimensionaler Verwackung. Rontgen Bl. 17 (1964) 126.
- REICHMANN S. (a) Development of spurious contours of spherical and cylindrical objects in tomography. Acta radiol. Diagnosis 12 (1972) 317.
- (b) Modified theory of the development of tomographic blurring. Acta radiol. Diagnosis 12 (1972) 457.
- WESTRA D. Zonography the narrow angle tomography. Excerpta Medica Foundation Amsterdam 1966.

RADIATION DOSE DISTRIBUTION IN TEMPORAL BONE TOMOGRAPHY

H DAHLIN, O NYLEN and H WILBRAND

Tomographic examination of the temporal bone is best performed with multi-directional movement: the one most widely used has hitherto been the hypocycloid. Small field sizes and a diaphragm close to the focus (STRÖM & BUCHMANN 1964, STRIEN 1968) contribute to improvement in the quality of the image as well as to local limitation and thereby reduction of the general radiation dose (JENSEN 1969). The exposure data required in ototomography (DAVIDSEN 1971) make great demands on the roentgen tube and involve relatively high radiation doses.

Only a few reports have been published concerning radiation dose measurements in connexion with tomographic examinations of the temporal bone. MUNDICH & FREY (1959) estimated the total gonadal dose in such examinations of the ear but failed to describe the mode of procedure. An estimation of skin and gonadal doses was made by JENSEN while the first practical dose measurements were performed with thermoluminescent dosimeters by ROVANO (1970) in his ototomographic investigations of otosclerosis. The use of thermo-



Fig. 1. Frontal and lateral aspects of the anatomically correct skull phantom for ototomography.

luminescence dosimetry for measuring radiation doses delivered to critical organs in association with temporal bone tomography was reported by CHRYSTOLL (1970) who also investigated the effect of lead lens shields on the doses absorbed by the lenses of the eyes.

The aim of the present investigation was to examine the radiation dose distribution to the different temporal bone structures and eye lenses with the five projections generally used in routine tomography of the temporal bone. Direct measurement of the dose distribution to different temporal bone structures in patients is not possible. A dose distribution curve may however be produced by means of radiation dose measurements in an anatomically and physically correct phantom. The dose delivered to deep temporal bone structures not accessible for direct measurement may thus be derived from those obtained in the external auditory meatus *in vivo*. The investigation thus consisted of two parts — measurements in a phantom and measurements in patients.

Methods and Material

Skull phantom. A complete skull served as the basic skeleton of the phantom with the possibility of exchanging the temporal bone for similar specimen from cadavers. The interior of the cranium was filled with Mix D with a mass density of 0.99, an electron density of 3.36 (JONES & RAINE 1949) and an effective atomic number of 7.42 (SPIERS 1946). The soft tissue of the skull and facial skeleton was modelled with silica paraffin wax with a mass density of 0.98, an electron density of 3.29 (HARRIS *et al.* 1956) and an effective atomic number of 7.3 (SPIERS 1946). The material was also used for modelling the soft tissues lining the air-containing spaces (Fig. 1). This phantom corresponds to the requirements of the International Commission on Radiologic Units and Measurements (ICRU report 10d 1962) and fulfils the demands (HUTTENLOCHER



Fig. 2. a) ototomogram) From the phantom with dosimeter chain in the sharply reproduced layer. LaF microrod dosimeters with intermediate steel pellets in teflon tubes. b) From patient with pair of dosimeters (LaF microcords) between steel pellets in teflon tubes in the external auditory meatus close to the ear drum.

et coll 1959) of an anatomic phantom for dosimetry with a volume of tissue equivalent material and reproduction of the human body both in external shape and radiophysical characteristics of its different components. It may also be used as an anatomic phantom for comparative diagnostic examinations (HEM VIKSSÖN 1971). For substitution of temporal bone specimens from different cadavers a corresponding part was removed from the phantom skull base; the deep frozen specimens were fitted into the corresponding defect and held in place with tissue equivalent material. Minor consequent defects in the bone continuity represented a source of error — probably negligible — in the evaluation of absorbed doses.

A small canal with a diameter of 2 mm was driven transversally through the otic capsule of the phantom with a burr drill under an operation microscope. The ear drum and the soft tissue of the external auditory meatus were removed making it possible for a chain of dosimeters to be inserted through the external meatus and exchanged for a new chain after tomographic exposure. Some disturbance in the mutual positions of the ossicles was unavoidable in drilling the dosimeter canal.

Dose measurements were made with five routine ototomographic projections bilaterally in six phantom mountings. 12 phantom ears were thus tomographed with 20 exposures per projection. The dosimetry in patients was performed in the external auditory meatus close to the ear drum. The examinations were made in 15 patients on a total of ten measurement occasions for each projection and with 8 to 26 exposures per projection. The corneal doses were measured at the same time both in the patients and the phantom.

Fig 3 a (top) Teflon catheter containing LiF microrods with intermediate steel pellets for ototomographic dosimetry in the phantom. b (middle) Teflon tubes containing pairs of LiF microrod dosimeters with steel pellet indicators for ototomographic dosimetry in a patient. (bottom) LiF teflon disc 12.7 mm in diameter and 0.4 mm thick for lens dose measurement on the eyelid of both the phantom and patients.



Thermoluminescence dosimetry was carried out both in the phantom and the patients. Dosimeters consisting of microrods 6 mm long and 1 mm in diameter (Isotopes Conrad MR LiF 7) were used in the temporal bone measurements.

For dose measurement in the phantom five microrod dosimeters were introduced through the external auditory meatus, contained in specially constructed teflon tubes (Fig 3 a, b) with steel pellets 1 mm in diameter placed in between the rods as indicators. The innermost dosimeter was thus situated in the lateral part of the internal auditory meatus and the following dosimeter lay in the inner ear, middle ear and the medial and lateral parts of the external meatus respectively (Fig 2a).

Dose measurements in the temporal bone structures in patient were made with a pair of dosimeters lying close to each other in a bent teflon tube located in the external meatus in the immediate vicinity of the ear drum (Fig 2b).

Measurements of corneal doses both in the patients and the phantom were obtained by means of disc shaped dosimeters with a diameter of 12.7 mm and a thickness of 0.4 mm (Isotopes Conrad D LiF-04) (Fig 3 c). According to BERGSTROM *et al.* (1972) there is no significant difference between the doses absorbed by the lens and by the cornea for the roentgen energy used. The values for corneal doses given in this report therefore apply also to those absorbed by the lens. The atomic numbers of LiF teflon and body tissue are so close that the values obtained may be considered to apply to the latter without correction.

The dosimeters must be preannealed for precision measurement. The preannealing process which gives thermoluminescent LiF good dosimetric properties must fulfil the following requirements (MARTENSSON 1969): (1) In a preannealing process all trapped electrons must return to the ground state of the crystal. (2) In the repeated use of dosimeters the preannealing process must be such that the glow curve is reproducible; this requires some of the stages of the crystals reaching thermal equilibrium during one phase of the preannealing procedure. MARTENSSON's work has suggested that for LiF teflon of a thickness

of 0.13 mm, 15 min at 300 °C is necessary to empty the filled traps completely. An appropriate glow curve giving low fading may be achieved by preannealing for about 20 hours at 80 °C (CARLSSON 1969). It was accordingly decided that the preannealing process should last 30 min at 300 °C followed by 20 h at 80 °C.

The results were read out in a Control for Radiation read-out instrument Model 7100 with a flow of nitrogen around the dosimeter for reduction of the background effect. The residual background signal was determined by means of five dosimeters taken at random from the dosimeters employed. The following read out cycle as recommended by CARLSSON was used. The dosimeter was placed in a read out position in a nitrogen atmosphere 30 s before the start of the read-out cycle. The read out took 15 s, but the dosimeter was retained in the read out position for a further 4 s.

The time after the read-out was reduced to 30 s for the microrod LaF teflon dosimeters. Every dosimeter used in the measurements was calibrated individually against a Farmer Secondary Standard dosimeter with 70 kV roentgen irradiation (2 mm Al filtration). As the dosimeters were heated before (30 min at 300 °C followed by 20 h at 80 °C) and after (30 min at 80 °C) the irradiation the signal read out was independent of time. The relative standard deviation of the mean varied for LaF teflon discs between 2.4 and 6.6 and for LaF teflon micro-rods between 2.3 and 5.6 per cent for each dosimeter irradiated on ten different occasions with ^{60}Co under reproducible geometric conditions.

A special dosimeter chain embedded in a cylindrical wax phantom was tomographed at a constant level in the most unfavourable projection to check the effect of the steel pellets on the individual dosimeter. The effect proved to be equal in the entire chain. The decrement of absorbed radiation in each dosimeter in relation to the preceding dosimeter was 5 to 10 per cent at the most.

Tomography was performed with hypocycloid movement on the Polytome, the focal size being 0.3 mm and the circular radiograph measuring 5 cm in diameter. Exposure data were 60 to 70 kV with 1 mm Al filtration, 50 mA, 11.6 s. The investigation included five routine ototomographic projections: Antero-posterior, half axial, axial, pyramidal, Sterners and lateral.

Both the ear lying uppermost and the one situated lowermost may be tomographed in the lateral projection. Dose measurements in the phantom were thus performed for both of these modes of examination. The tomographic examination and dose measurement in the patients comprised only the lowermost ear.

Seventy-two dose measurements were performed with the phantom in a corresponding number of tomographic series with a total of 1440 exposures. Fifty such measurements were performed in a corresponding number of tomo-

Table 1

Absorbed dose in roent in otoscopy in phantom

Projection	External meatus lateral part	External meatus medial part	Middle ear	Inner ear	Internal meatus	Ipsilateral lens	Contralateral lens
<i>Anteroposterior</i>							
Mean value	270	160	110	79	67	690	14
Range	9-435	71-355	65-140	47-186	44-107	356-107	4.0-21
<i>Half axial</i>							
Mean value	68	71	87	64	74	1060	700
Range	44-88	51-100	48-188	55-94	60-135	520-1330	474-1590
<i>Anal pyramidal</i>							
Mean value	45	55	63	53	64	13	630
Range	14-70	35-83	44-96	40-143	53-156	7.0-18	100-1115
<i>Stenvers</i>							
Mean value	1540	990	470	265	160	9.2	4.2
Range	915-2205	455-2250	195-1221	67-897	55-299	5.9-17	1.0-12
<i>Lateral (up)</i>							
Mean value	1740	1050	490	260	140	4.8	4.7
Range	685-3321	425-2515	230-1020	78-332	31-242	2.0-11	1.0-11
<i>Lateral (down)</i>							
Mean value	23	27	26	40	70	4.5	4.9
Range	14-57	20-58	23-40	26-66	53-112	2.0-12	4.0-70

graphic series with a varying number of exposures in different patients (total 905 exposures)

Results

Table 1 gives the values obtained in the phantom for the absorbed doses in the temporal bone structures and the ipsi- and contralateral lens doses in routine projections. There was a marked difference in dose distribution between the two modes of tomography in the lateral projection: the one with the tomographed ear near the radiation source and the other with the tomographed ear near the film. It is easier to tomograph the accessible uppermost ear and it appears to be the routine in many centres. The difference in absorbed dose between the two modes of examination corresponded to a factor of 10 to 15: the dose absorbed by the lens varied, of course, with the projections.

Table 2

Standard dose in steel in otomography in patients

Projection	External meatus lateral part (mea- sured)	External in situ medial part (mea- sured)	Middle ear (cal- culated)	Inner ear (cal- culated)	Internal meatus (cal- culated)	Ipsilateral lens (mea- sured)	Contralateral lens (mea- sured)
Anteroposterior							
Mean value	180	110	71	57	43	900	16
Range	92-474	56-290	37-190	27-139	23-120	85-1277	1.9-48
Half axial							
Mean value	115	120	140	105	105	1330	590
Range	59-193	40-198	17-250	35-17	36-178	756-2126	105-1815
Axial pyramidal							
Mean value	43	51	57	46	50	73	780
Range	33-58	37-66	41-74	33-59	36-6	17-761	178-1500
Stenvers							
Mean value	1070	670	310	165	105	13	5.5
Range	507-1772	317-1110	147-512	78-272	50-173	4.7-46	1.6-23
Lateral							
Mean value	17	21	21	31	53	2.2	4.1
Range	4.3-28	5.2-34	3.2-33	7.7-49	12-71	1.2-3.9	1.7-3.6

Because of anatomic differences between the phantom specimens the value obtained at each individual measurement in each projection was standardized to the value for the lateral part of the external meatus in order to attain equivalence between the different conditions. The value measured in the external meatus was therefore set to 100 per cent. The standardized values formed the basis for construction of a relative dose distribution curve for each projection. These curves appear in Figs 4 to 9 against a background of a schematically drawn temporal bone tomogram containing a dosimeter chain. The geometrically defined position of each dosimeter between steel pellets in relation to its structural environment in the temporal bone appears in the graphic representation. The typical variations in dose distribution to the temporal bone structures in each projection are indicated by the dashed line.

It was thus possible to calculate the dose delivered to inaccessible structures of the temporal bone in the patients by means of this dose distribution curve. Table 2 gives the values obtained in these calculations. The highest dose values were reached for Stenvers and the half axial projection, while in the others they were considerably lower.

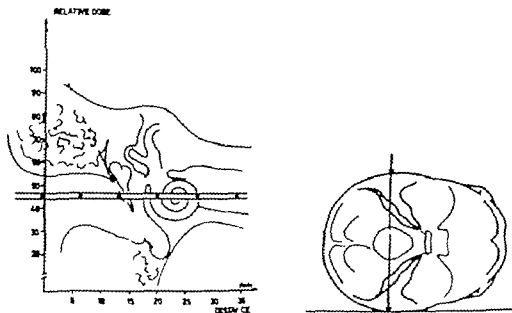


Fig. 8 Lateral projection (the tomographed measured ear is near to the radiation source) with radiation dose distribution to temporal bone structures. No marked difference from the distribution in the a.p. and Stenvers' projections evident.

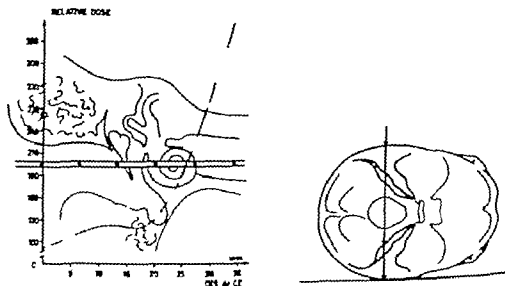


Fig. 9 Lateral projection (the tomographed measured ear is next to the film) and radiation dose distribution to temporal bone structures. In contrast to all other projections the dose distribution curve represents a considerable decrease in the radiation doses laterally from the internal auditory meatus to the inner ear and further to the middle ear and external auditory meatus.

Tables 1 and 2 indicate high dose values for the eye lens on the ipsilateral side in the a p and half axial projections as well as on the contralateral side in the axial pyramidal projection

Discussion

Radiation exposure dose measurements in tomography of the ear with hypocycloid movement on the Polytome were made by MURDOCH & FREY (1959) who recorded a total gonadal exposure of 0.5 to 3.0 R in a series of 25 cuts. With equipment and exposure conditions similar to that of the present authors JENSEN estimated a total gonadal dose of 30 mR in 35 ototomographic exposures in children and unmeasurably low values with normal protection of the abdomen. Both ROVINSO and CHAN *et coll.* confirmed low gonadal doses.

ROVINSO estimated the doses absorbed by temporal bone structures by measurements in the external meatus. CHAN *et coll.* measured radiation doses in the middle ear in a phantom and in the external meatus in patients. Our intention was to investigate the dose distribution to the inner and middle ear in tomography of the temporal bone and thus the distribution to presumptive critical organs. These include sensory structures, the vascular apparatus controlling the intricate balance between endo- and perilymphatic fluids, the specific vascularization system of the ossicles and the delicate mucoperiosteal tissue of the middle ear.

ROVINSO employed thermoluminescence dosimetry with separate dosimeter samples in the external meatus and obtained average values of 500 mrad (range 220 to 800 mrad) in 49 exposures with different projections. He recorded an exponential increase in the dose towards the ear drum and calculated that an average dose of 5 rad would be delivered to bone tissue in the lateral wall of the labyrinth. In contrast to ROVINSO who measured the absorbed doses throughout a tomographic examination including several projections, the present authors investigated the dose distribution in each projection separately. It may be pointed out that there was no change or any marked increase in absorbed doses towards the inner ear except for the lateral down projection (Figs 4 to 9).

If 24 to 36 exposures be regarded as average for a simple routine tomographic examination of the ear the present results represent a mean dose value of 3 to 4 rad to middle and inner ear structures.

Little is known about the radiation sensitivity of the inner and middle ear structures. This is due to the difficulties in gaining access to these structures both in clinical and experimental examinations. As early as 1905 EWALD described radiation effects on auditory structures—a communication that was soon

followed by a few reports on the direct therapeutic effects of irradiation of tumours of the skull and cervical regions. Both clinical and experimental investigations have revealed gross and microscopic changes or functional alterations after exposure doses from several 100 to several 1 000 R. WITTNER (1970) described submicroscopic, experimental irradiation effects on sensory structures of the inner ear in guinea pigs. Degeneration of sensory cells was observed in the cochlea after roentgen irradiation with 4 000 R and more, and in the vestibular part of the labyrinth after irradiation with 6 000 R and more. The effect of repeated minor doses over a long period of time is a matter of clinical interest. Apart from effects on sensory structures, which appear to have a relatively high resistance to irradiation, there is no information about radiation biologic effects on other submicroscopic structures in the inner or middle ear. Against the background of our poor knowledge on such influences on auditory structures, dose values of 3 to 4 rad may be regarded as not seriously harmful to sensory tissue components of the ear. No national or international recommendations have been made as to the highest permissible dose that should be delivered to different organs in roentgenographic examinations. For those continuously exposed to ionizing radiation in their work, the maximum permissible dose equivalent to structures such as the temporal bone is 15 rem/year (ICRP 1970).

It may be pointed out that the difference between energy absorption in bone and soft tissue is of special interest in bone cavities containing soft tissue. JONES & CUNNINGHAM (1970) stated that a dose 50 per cent greater than the soft tissue value is obtained for photon energies of 50 keV in a 100 micron cavity of bone marrow; the excess dose is about 14 per cent for a 400 micron cavity. The variation in dose with photon energy has a peak at about 50 keV. The doses absorbed by small soft tissue containing bone cavities in temporal bone structures are thus higher than those estimated in this investigation.

In spite of the beam concentration on ear structures in temporal bone tomography the highest absorbed doses are not localized to these structures. Tables 1 and 2 indicate that the eye lens doses are markedly high, the wide range in the values being due to the distance between the two eyes, which varies from one patient to another, as well as the other anatomic factors. The eye lens doses are especially unfavourable in a p half axial and axial pyramidal projections. These projections are frequently used because of their high information value from the diagnostic point of view. If 10 exposures be regarded as average for these projections an ipsilateral lens dose of 15 rad and a contralateral dose of 8 rad may be assumed in a routine unilateral ototomographic investigation. The eye lens doses must be considered in the light of the finding of lens opacities in experimental animals after an exposure of 15 R (USTON *et al.* 1956) and of cataract in adults after an exposure of 200 R (MERIAM & FOCHT 1957).

Conclusions

The time consuming procedure of tomography of the ear demands detailed planning in every individual instance. The choice of projections depends upon the information requested. In examinations before plastic or reconstructive middle ear surgery or for investigation of malformations a detailed report is required and the procedure will thus be more extensive. Information is the essential aim in planning but radiation hygienic factors must be stressed in the choice of the projections and number of exposures. Tomography in the lateral projection should for instance be performed with the tomographed ear near to the film for the sole object of radiation protection. High radiation doses are required to produce effects on sensory structures in the inner ear and the doses delivered at ototomography are in this respect negligible. Little is known however concerning radiation effects on other structures and functions of the ear for example the influence on the mechanism of balance between the endo- and perilymphatic spaces and on the specific vascularity of the otic capsule and vessels: the question of radiation hazards must, therefore, always be considered. Concerning these structures the radiation effects on soft tissue in small bone cavities (JOHNS & CUNNINGHAM 1970) should be taken into account.

The eye lens doses require greater consideration in ototomography than the doses to otic structures from the radiation hazard viewpoint. The doses absorbed by the lens necessitate the use of lens shields, as already pointed out by CAMM et al. The results of lens dose measurements in different projections indicate that the use of lens shields in the a.p. half axial and axial pyramidal projections is of value, while such protection in Stenvers and the lateral projection is practically useless.

Acknowledgement

The authors take this opportunity of thanking Björn Bergström for his valuable help in the otosurgery necessary for this investigation.

SUMMARY

The radiation dose distribution to middle and inner ear structures in ototomography was investigated by means of thermoluminescence dosimetry in phantom and curves constructed for each individual projection. The doses in patients are estimated with the aid of the dose distribution curve by extrapolation by means of values obtained in the external meatus. The dose values obtained are discussed in the light of previously reported findings.

ZUSAMMENFASSUNG

Mit Hilfe der Thermolumineszenzdosimetrie wurde die Strahlendosisverteilung auf Mittel- und Innenohrstrukturen bei der Ohrtomographie am Phantom untersucht. Auf diese Weise wurde die Konstruktion einer Dosisverteilungskurve für jede einzelne Projektion ermöglicht. Damit konnten die Absorptionsdosen der Mittel- und Innenohrstrukturen durch Extrapolierung in Anlehnung an die im äußeren Gehörgang ermittelten Werte errechnet werden. Die Ergebnisse der Dosismessungen werden mit Hinblick auf die jetzigen Kenntnisse besprochen.

RÉSUMÉ

La distribution de dose de radiation aux structures de l'oreille moyenne et interne au cours de l'otomographie a été étudiée par la dosimétrie de thermoluminescence sur un fantôme et une courbe a été construite pour chaque incidence tomographique. Les doses sur des malades ont été estimées au moyen de la courbe de distribution de dose par extrapolation à partir de valeurs obtenues dans le conduit auditif externe. Les valeurs de dose obtenues sont examinées à la lumière des résultats publiés auparavant.

REFERENCES

- BERGSTRÖM K., DAHLIN H., GUSTAFSSON M. and NYLEN O.: Eye lens doses in carotid angiography. *Acta radiol. Diagnosis* 12 (1972) 134.
- CARLSON C. A.: Thermoluminescence of LiF . Dependence of thermal history. *Phys. in Med. Biol.* 14 (1969) 107.
- GUN F. K., ANDERSON W. B. and GILBERTSON J. D.: Radiation dose to critical organs during petrous tomography. *Radiology* 94 (1970) 623.
- DAVIDSON H. G. Jr: Fundamentals of ear tomography, p. 1. Edited by J. Jensen and H. Rosner. Charles C. Thomas, Springfield, Ill. 1971.
- EALD C. A.: Die Wirkung des Radiums auf das Labyrinth. *Z. Physiol.* 19 (1903) 797.
- HARRIS J. H., TUDENHAM W. J., STANTON L. et coll.: The development of a chest phantom for use in radiologic dosimetry. *Radiology* 67 (1956) 805.
- HENNINGSON A.: Cervical phantom for evaluation of different methods of roentgen examination of the larynx. *Acta radiol. Diagnosis* 11 (1971) 515.
- HULTBERG S., DAHLIN O., THORAEUS R. et coll.: Halocure cobalt 60 therapy: the Radium beamster. *Acta radiol.* (1959) Suppl. No. 179.
- ICRP: Recommendation of the International Commission on Radiological Protection. Publication 9. Pergamon Press, London, 1966.
- ICRU: Report 10 b: Physical aspects of irradiation. NBS Handbook 85. National Bureau of Standards, Washington, D.C. 1962.
- Report 10 d: Clinical dosimetry. NBS Handbook 87. National Bureau of Standards, Washington, D.C. 1962.
- JENSEN J.: Malformations of the inner ear in deaf children. A tomographic and clinical study. *Acta radiol.* (1969) Suppl. No. 286.
- JONES D. E. A. and RAYNE H. C.: Letter to the Editor. *Brit. J. Radiol.* 22 (1949) 549.
- JONES H. E. and CURRY JAW J. R.: The physics of radiology, p. 457. Charles C. Thomas, Springfield, Ill. 1970.

- MARTENSON B. Thermoluminescence of LiF - statistical analysis of the influence of pre annealing on the precision of measurement. *Phys. in Med. Biol.* 14 (1969) 119
- MARRIAM G. R. and FOCURT E. F. A clinical study of radiation cataracts and relationship to dose. *Amer. J. Roentgenol.* 77 (1957) 759
- M. VONCH K. und FAHY K. W. Das Röntgenlichtbild des Ohres. Georg Thieme Stuttgart 1959
- ROVINGO H. Otosclerosis. A tomographic-clinical study. *Acta radiol.* (1970) Suppl. No. 296
- SPITZ F. W. Effects of atomic number and energy absorption in tissues. *Brit. J. Radiol.* 19 (1946) 52
- STRIKE F. E. Bevorzugte Darstellung einzelner Körperschichten. In: *Handbuch der Medizinischen Radiologie* Band III S. 813 Springer Berlin Heidelberg New York 1967
- STROHM CH., BUCHMANN F. und SCHNEIDER S. Der Einfluss der Einblendung auf die Detailerkennbarkeit im Schichtbild. *Röntgen Bl.* 17 (1964) 442
- UPTON A. C., CHASTREVEAU K. W., MILLER G. S. et coll. The relative biological effectiveness of neutrons, X rays and gamma rays for the production of lens opacities. Observations on mice, rats, guinea pigs and rabbits. *Radiology* 67 (1956) 686
- WETTER F. O. X ray irradiation of the inner ear of the Guinea pig. Universitetsforlaget Oslo 1970

Book review

RADIOLOGY OF THE SKULL AND BRAIN Volume 1 The Skull Edited by T H Newton and D G Potts 873 pages (2 books) with 2314 illustrations C V Mosby St Louis 1971 Price \$78.50

These two books composing the first volume in a set of three are best presented by quoting the editors' preface. The set is intended to be a reference source for those training in the fields of neuroradiology, neurology and neurosurgery as well as for the experienced radiologist and clinician. Many authors who have contributed to the expanding knowledge in the field of neuroradiology have been invited to share in the writing of the three volumes: volume 1 on the skull, volume 2 on angiography and volume 3 on pneumography, neuropathology and isotopic and other techniques. Each volume contains a section devoted to a discussion of the technical problems related to a particular examination as well as the gross and radiologic anatomy, and when indicated separate chapters are devoted to a detailed analysis of the roentgen features of specific pathologic entities.

The first volume after an introductory historical survey consists of 8 parts: technical aspects of skull roentgenography, skull maturation, skull vault, skull base (book 1), orbit, congenital anomalies, metabolic diseases and other diseases involving the skull (book 2), the last part including a large section on trauma. Each part in turn is made up of several chapters covering different aspects of the topic, each being provided with an extensive list of references.

The illustrations are as a rule of an excellent quality; in particular the liberal use of anatomic specimens is a good feature. In general the supply of illustrations is generous and judiciously selected, with occasional detours into the fields of cartoons or pre-Columbian pottery. A certain amount of overlapping between different chapters is probably unavoidable with the logical organization of the material used, but it does not reach a disturbing level. Much concern has obviously been given to the large subject index, which is duplicated at the end of each book.

It is no easy task to give an impartial review of such an encyclopedic work, the value of which is best tested by its use as a source of reference in the daily routine. Having done this for some time, I have been particularly impressed by the part on skull base containing no less than seven separate chapters. This book sets a standard hitherto unsurpassed and the decision of the editors to leave out the spine and the spinal cord, perhaps to be regretted if understandable. The next two volumes are eagerly awaited.

Ulf Bergvall

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AORTOCERVICAL INTERNAL CAROTID AND VERTEBRAL ANGIOGRAPHY IN TOTAL CEREBRAL INFARCTION

E. O. JØRGENSEN

A decrease in systemic blood pressure and heart rate may occur during cerebral angiography in patients with a normal brain circulation (GERTZ 1956, LUNDEG-
VOLD & ENOSET 1969). It has been suggested that these haemodynamic changes
result in a slower passage of contrast medium through the brain (FISCHER &
LEKSTEN 1961) although this aspect has apparently not been explored in
possible total cerebral infarction. Changes in the systemic blood pressure and
heart rate during aortocervical internal carotid and vertebral angiography
were therefore investigated and the influence of such changes on the passage of
the medium in patients with total cerebral infarction evaluated.

Material and Methods The 10 patients examined consisted of 6 with traumatic
brain lesions, 1 with spontaneous intracranial haemorrhage, 1 with cerebral
embolism and 2 with circulatory and respiratory arrest. Aortocervical angio-
graphy was performed in all patients while 7 patients had additional unilateral
internal carotid and vertebral angiography.

Forty ml Urografin 76 % were injected into the ascending aorta at a flow
rate of 30 ml/s by means of a pump (Contrac) through a catheter inserted into

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the femoral artery and serial films of the neck and skull obtained with a rapid film changer. This procedure was repeated after 20 or 40 minutes, 14 films being exposed at intervals of 0.5 to 6 s over 24 s in the first and over 127 s in the second series. For the selective injections the right internal carotid and vertebral arteries were usually catheterized. 10 ml medium were injected at a flow rate of 5 ml/s and 14 films exposed at 0.5 to 6 s over 54 seconds.

A 16 channel minograf (Elema) monitored the electrocardiogram aortic blood pressure (through a separate catheter) artificial respiration duration of the injection of the medium and exposure sequence during the angiography. The indication for angiography was possible total cerebral infarction suggested by a flat EEG and cranial nerve reflexes (JORGENSEN & BRODERSSEN 1971). The EEG was considered flat when it presented no cortical activity above 2 mV (corresponding to the nose level) during 30 min of recording (JORGENSEN 1971). Patients were classified as being without cranial nerve reflexes when pupillary caloric vestibular coughing swallowing and respiratory reflexes could not be elicited and when no change in heart rate could be induced by eye ball and carotid sinus pressure. Spinal reflexes were present in all patients: half of them developed unilateral flexion reflex of the lower limb and unilateral extension/pronation reflex of the upper limb characteristic of total cerebral infarction (JORGENSEN & BRODERSSEN).

At angiography 2 to 8 hours after cortical activity in the EEG and cranial nerve reflexes had disappeared all patients required artificial respiration and infusion of pruroxamine. This was performed at a mean aortic blood pressure (aorta MBP) of over 65 mm Hg. The artificial respiration was interrupted during the exposures to avoid movements of the head. Before this the patient had been hyperventilated with 50 per cent oxygen.

Results

Aorticercical angiography. An increase in the aorta MBP from 5 to 15 mm Hg always occurred during the injection of contrast medium and in the following 4 s. No change in heart rate was associated with this rise in systemic blood pressure. Subsequently the aorta MBP decreased either after more than 10 s accompanied by a slight decrease in heart rate (response A) or within 10 s accompanied by cardiac arrhythmus (response B).

Response A. The 8 patients responded uniformly on nineteen injections of contrast medium into the aortic arch. At 10 s the aorta MBP ranged from 10 mm Hg above to 5 mm Hg below the preangiographic mean pressure. At 30 s the aorta MBP had decreased by 15 to 15 mm Hg. The blood pressure returned to the preangiographic level at 38 to 100 s (mean 63 s SD 24 s).

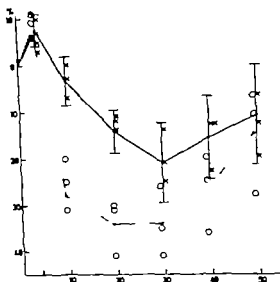


Fig 1 Changes in aorta MBP during aortocervical angiography in possible total cerebral infarction. Abscissa time in seconds after injection of contrast medium ordinate changes in percentage of preangiographic aorta MBP. Solid line response A. A crage of nineteen injections in 8 patients. Vertical bars $SD \times 2$. Patients premedicated with tropine. Broken line response B. A crage of three injections (closed circles) in 2 patients.

The preangiographic mean pressure in the aorta varied from 63 mm to 147 mm Hg in different patients. The changes in aorta MBP were determined as the percentage of the preangiographic aortic mean pressure (Fig 1).

The heart rate decreased 1 to 9 beats/min during angiography; it returned to its preangiographic frequency within 23 to 80 s in half the patients but in the other half it remained 1 to 2 beats/min slower. Identical changes in systemic blood pressure and heart rate were observed after injection of 40 ml physiologic saline at a flow rate of 30 ml/s in 2 patients. Premedication with atropine (0.05 mg/kg) in 4 patients did not influence the haemodynamic responses to the injection of medium (Fig 1).

The consequences of interrupting the artificial respiration during angiography were investigated in 4 patients. The heart rate remained constant during 1 min of apnea but the aortic mean pressure decreased linearly by 5 to 15 mm Hg; however injections of medium caused a decrease in the systemic blood pressure which was three times more marked at 30 s than the maximal decrease in pressure induced by apnea.

Response B. Two patients had a fall in blood pressure within 10 s following three injections of medium and in addition developed cardiac arrhythmia. The decrease in aorta MBP was 21 to 50 mm at 10 s and 22 to 69 mm at 30 s. The average decrease in percentage of the preangiographic aorta MBP at 10 s was eight times more marked than in patients with response A (Fig 1). The aorta MBP returned to the preangiographic level at 55 to 71 s.

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At angiography 2 to 8 hours after cortical activity in the EEC and cranial nerve reflexes had disappeared, all patients required artificial respiration and infusion of pressor amines. This was performed at a mean aortic blood pressure (aorta MBP) of over 65 mm Hg. The artificial respiration was interrupted during the exposures to avoid movements of the head. Before this the patient had been hyperventilated with 50 per cent oxygen.

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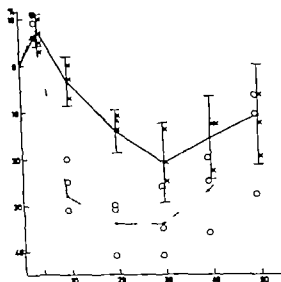


Fig. 1 Changes in aorta MBP during aortocervical angiography in possible total cerebral infarction. Abscissa: time in seconds after injection of contrast medium. Ordinate: changes in percentage of preangiographic aorta MBP. Solid line: response A. A range of nineteen injections in 8 patients. Vertical bars: $SD \times 2$. \times : Patients premedicated with tropine. Broken line: response B. A range of three injections (closed circles) in 2 patients.

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Response B. Two patients had a fall in blood pressure within 10 s following three injections of medium and in addition developed cardiac arrhythmias. The decrease in aorta MBP was 21 to 50 mm at 10 s and 22 to 69 mm at 30 s. The average decrease in percentage of the preangiographic aorta MBP at 10 s was eight times more marked than in patients with response A (Fig. 1). The aorta MBP returned to the preangiographic level at 55 to 71 s.

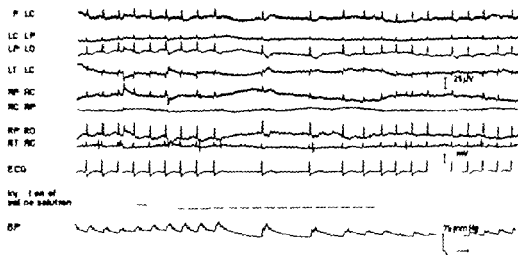


Fig. 2. EEC, ECG and aortic blood pressure after injection of 40 ml normal saline into the aorta. During the first 4 s the aortic MBI increased from 91 to 106 mm Hg, the pressure then decreased to 10 to 65 mm Hg and to 25 s to 47 mm Hg. EEC: Prolonged R-R intervals from the 2nd to the 8th second. EEC: Extracerebral signals only (50 Hz AC, EEC and disturbances due to movements of the head during the aortic injection).

Bradycardia appeared 1 to 5 s after each injection in one of the 2 patients; the heart rate decreasing 30 to 40 beats/min for 4 to 13 s. The duration of bradycardia varied in direct proportion to the preangiographic systemic mean blood pressure (91 to 169 mm Hg); also the longer the bradycardia lasted the longer was the fall in systemic blood pressure (55 to 71 s). After each angiography the heart rate had decreased by 2 beats/min.

The other patient had ventricular premature beats from the 5th to the 15th second after the termination of the injection of medium.

Response B could be reproduced by the injection of phlebographic saline (Fig. 2).

Internal carotid angiography. Seven patients had internal carotid angiography. Injections of contrast medium or saline reproduced the late fall in blood pressure with minor changes in heart rate (response A) in 5 patients and early fall in blood pressure with cardiac arrhythmia (response B) in the other 2 patients with the same response to aortic injections.

Vertebral angiography. The 7 patients mentioned had vertebral angiography following internal carotid angiography. Contrary to the findings during aortocervical and internal carotid angiographies, no fall in the systemic blood pressure

T ble

Haemodynamic responses to aortic and internal carotid injections related to an angiographic finding.

Response	Angiography					
	Aortocervical		Internal carotid		Vertebral	
	N of cases	Infra tentorial circulation	N of cases	Infra tentorial circulation	N of cases	Infra tentorial circulation
A	8	0	5	0	5	0
B	2	0	2	1	2	2

A Fall in aorta MBP after 10 s accompanied by slight decrease in heart rate

B Fall in aorta MBP within 10 s accompanied by cardiac arrhythmia

Same patients

sure and only minor changes in heart rate if any occurred after the injection of contrast medium or saline into the cerebral artery

Of 5 patients with response A to aortic and carotid injections 3 had a constant aorta MBP and 2 patients a rise in aorta MBP of 5 and 18 mm during 60 and 77 s respectively. The heart rate decreased 1 to 3 beats/min. In the 2 patients with response B during aortocervical and internal carotid angiographies no change in blood pressure or heart rate occurred during vertebral angiography.

Haemodynamic responses related to angiographic findings: The results are summarised in the Table. Aortocervical angiography in patients with response A disclosed arrested flow of contrast medium in the internal carotid and vertebral arteries at the level of C2 to C5. Medium was retained in the initial parts of the intracranial arteries for more than 50 s in patients with response B. None of the aortocervical examinations revealed any filling of the intracranial veins.

Internal carotid and vertebral angiographies in 5 patients with response A indicated an inflow of medium into the initial parts of the intracranial arteries but no venous filling.

The two patients with response B had an inflow of contrast medium into the initial parts of the supratentorial arteries after internal carotid injections and filling of the infratentorial arteries with vertebral injections. Neither of them had supratentorial venous filling. Outlining of the infratentorial veins occurred in one patient at 14 s on internal carotid angiography (Fig. 3) but both had infratentorial venous filling after 21 to 24 s with vertebral angiography (Fig. 4).

Total cerebral infarction was considered to have taken place when the cerebral circulation had been blocked for 20 min at a body temperature above 30 °C.



Fig. 3. Internal carotid angiography. a) Four seconds after injection of contrast medium with inflow into the proximal parts of the middle cerebral and posterior communicating arteries. b) 14 seconds later filling of the veins in the posterior fossa. Supratentorial circle outlined.

and for 40 min at temperatures below 30°C (JØRGENSEN & BRODENSEN). The time limits correspond to twice the duration of ischaemia incompatible with cerebral recovery in animals at the temperatures mentioned (BOKONJI, 1963).

Cerebral angiographies in possible total cerebral infarction often revealed inflow of contrast medium with retention in the intracranial arteries. An absence of filling of the veins was therefore considered proof of an arrest of circulation. Since such an arrest might be due to the unavoidable fall in systemic blood pressure following aortic and internal carotid injections, special attention was paid to the vertebral angiographies, which did not induce any decrease in systemic blood pressure. Patients without filling of the intracranial veins on vertebral angiographies performed 20 or 40 min apart were declared brain dead. They all had haemodynamic responses of type A to aortic and internal carotid injections.

The two patients with filling of the infratentorial veins could not be considered brain dead. The extremely slow circulation in the posterior fossa was sufficient to maintain some brain stem function, as one of the patients regained gasping respiratory movements during angiography. Moreover the haemodynamic response of type B to aortic and internal carotid injections should be considered indicative of brain stem function. One of these patients had irreversible circulatory arrest 2 hours after the roentgenologic examination. The internal carotid and vertebral angiographies were repeated in the other patient 18 hours later, then the heart rate decreased 1 to 2 beats/min but the systemic blood pressure did not change after vertebral injections. Carotid injections however caused



Fig. 4. Vertebral angiography. Same patient as in Fig. 3. a) Four seconds after injection of medium. Infratentorial arteries: the posterior communicating and the internal carotid arteries filled. b) 21 seconds later. Venous filling in the posterior fossa.

alterations in systemic blood pressure and heart rate of type A. No filling of the intracranial veins ever occurred.

Discussion

One of two haemodynamic responses to aortic and internal carotid injections occurred in possible total cerebral infarction depending upon whether or not any infratentorial circulation was present. Without such circulation a decrease in systemic blood pressure began at more than 10 s and was most marked after 30 s as in spinal animals after bilateral vagotomy or heavy atropine administration (LUNDGREN & TORNELL 1958). In addition patients without brain circulation had a decrease in heart rate of 1 to 9 beats/min.

Subjects with a slow infratentorial circulation had a marked decrease in systemic blood pressure within 10 s and the lowest pressure after 20 to 30 s. The fall in pressure was accompanied by cardiac arrhythmia as described in animals and man with a normal brain circulation (FISCHER & EASTEN 1961; GRUETZ 1956; HILAL 1969; LUNDGREN & TORNELL 1958; LUNDERVOLD & ENGESSET 1969). However in patients with a slow infratentorial circulation the fall in systemic blood pressure lasted twice as long as in those with normal perfusion of the brain.

In contrast to the findings during aortocervical and internal carotid angiographies injections of contrast medium or physiologic saline into the vertebral artery did not induce any decrease in systemic blood pressure regardless of the state of the infratentorial circulation.

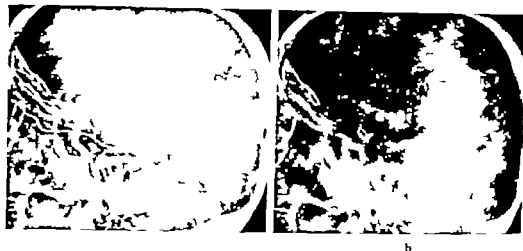


Fig. 3 Internal carotid angiography. a) Four seconds after injection of contrast medium with inflow into the proximal parts of the middle cerebral and posterior communicating arteries. b) 14 seconds later filling of the veins in the posterior fossa. Supratentorial cisterns not outlined.

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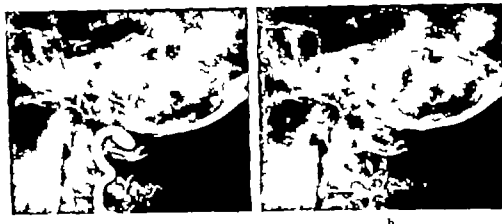


Fig 4 Vertebral angiography Same patient as in Fig 3 a) Four seconds after injection of medium Infratentorial arteries the posterior communicating and the internal carotid arteries filled b) 1 seconds later Venous filling in the posterior fossa

alterations in systemic blood pressure and heart rate of type A. No filling of the intracranial veins ever occurred.

Discussion

One of two haemodynamic responses to aortic and internal carotid injections occurred in possible total cerebral infarction depending upon whether or not any infratentorial circulation was present. Without such circulation a decrease in systemic blood pressure began at more than 10 s and was most marked after 30 s as in spinal animals after bilateral vagotomy or heavy atropine administration (LUNDQVIST & TORNELL 1958). In addition, patients without brain circulation had a decrease in heart rate of 1 to 9 beats/min.

Subjects with a slow infratentorial circulation had a marked decrease in systemic blood pressure within 10 s and the lowest pressure after 20 to 30 s. The fall in pressure was accompanied by cardiac arrhythmia as described in animals and man with a normal brain circulation (FISCHER & EASTEN 1961; GREITZ 1956; HILAL 1969; LUNDQVIST & TORNELL 1958; LUNDQVIST & ENGSET 1969). However in patients with a slow infratentorial circulation the fall in systemic blood pressure lasted twice as long as in those with normal perfusion of the brain.

In contrast to the findings during aortocervical and internal carotid angiography, injections of contrast medium or physiologic saline into the vertebral artery did not induce any decrease in systemic blood pressure regardless of the state of the infratentorial circulation.

ZAREBOK *et coll* (1954) stated that patients with a normal brain circulation respond to aortic injections of any hypertonic solution with a fall in blood pressure. GREITZ (1956) reported that the fall in pressure could usually not be reproduced by injection of physiologic saline. The contrast media have therefore been thought to stimulate extracerebral chemoreceptors (ZAREBOK *et coll*) vasomotor areas in the brain (GREITZ 1956; HILAL 1969; LINDQVIST & TONELL 1958) or peripheral vasodilators (HILAL 1969). An effect on baroreceptors was considered of minor significance.

The aortic and internal carotid injections of both contrast medium and physiologic saline in the present investigation produced a rise in systemic blood pressure of 5 to 15 mm and of 5 to 10 s duration. This initial rise in blood pressure probably stimulated aortic and carotid stretch receptors and elicited a reflexive fall in systemic blood pressure. In patients without brain circulation the late fall in pressure with slight changes in heart rate were probably due to peripheral vasodilatory reflexes. As the haemodynamic response was unaltered after premedication with atropine it is likely that sympathetic vasomotor nerve fibres insensitive to the drug constituted the efferent pathway (LINDQVIST 1955). In the two patients with extremely slow infratentorial circulation the early and marked fall in blood pressure, accompanied by cardiac arrhythmia, was considered of vagal origin: a similar response occurs in those with intact vagal reflexes.

It would appear that the total arrest of the cerebral circulation in total cerebral infarction may be exclusively explained by increased intracranial pressure when this pressure approximates the systemic blood pressure the perfusion of the brain falls towards zero (MITCHELL *et coll* 1967) and the contrast medium fails to pass the brain. Thus the findings in cerebral angiography are determined by the difference between the systemic blood and intracranial pressures termed the perfusion pressure (ZWIETANOV 1970).

The rise in systemic blood pressure following the injections of contrast medium that occurred in the present aortocervical and internal carotid angiographies accounted for an initial increase in the perfusion pressure indicated by an arterial inflow of medium; however the following unavoidable fall in blood pressure and consequent reduction in the perfusion pressure may jeopardize the outlining of cerebral veins. This conception was supported by the finding of infratentorial venous filling at vertebral angiography, a procedure that did not induce a fall in systemic blood pressure in subjects without demonstration of the veins at aortocervical and internal carotid angiographies.

The absent supratentorial but definite infratentorial venous filling at internal carotid angiography in one patient (Fig. 3) illustrates that local differences in pressure may exist intracranially.

The dissociation between the findings at aortocervical and at internal carotid

and vertebral angiographies in possible total cerebral infarction has been reported previously (HEISKANEN 1964 BLICHLER et coll 1970 VLAHOVITCH et coll 1971) but was explained as a result of the injection of different amounts of medium at various injection pressures. Haemodynamic changes during the cerebral angiographies were not taken into consideration.

Contrast medium normally passes the brain in less than 10 s (Gætz 1956).

Haemodynamic reflexes and spontaneous respiration indicative of a functioning brain stem, were observed in patients with infratentorial venous filling at 14 to 21 s in the present material. As long as the delay in venous filling compatible with a living brain is unknown, a virtual absence of filling of the brain veins must be required for the diagnosis of total cerebral infarction. As aortic and internal carotid injections induce a fall in systemic blood pressure which may influence the passage of contrast medium through the brain, vertebral angiography is considered superior for the demonstration of the arrest of the intracranial circulation in total cerebral infarction.

Acknowledgement

This investigation was supported by grants from the P. Carl Petersen Foundation and the Danish Heart Foundation.

SUMMARY

Aortic and carotid injections of contrast medium elicited significant decreas in the systemic blood pressure with or without arterial arrhythmia in subjects with possible total cerebral infarction; this was dependent upon whether or not any infratentorial circulation was present. Vertebral angiography induced no decrease in the systemic blood pressure and may therefore be recommended for the detection of complete arrest of the cerebral circulation.

ZUSAMMENFASSUNG

Eine Kontrastmittelinjektion in die Aorta oder Carotis führt zu einem signifikanten Abfall des Blutdrucks im Systemkreislauf mit oder ohne Herzarrhythmie bei Personen mit einem wahrscheinlichen Gehirnstod. Dieses Verhalten ist davon abhängig, ob eine infratentorielle Zirkulation vorhanden ist oder nicht. Eine Vertebroangiographie rief keinen Abfall des Blutdrucks im Systemkreislauf hervor und kann daher empfohlen werden, um einen vollständigen Stillstand der Gehirnzirkulation festzustellen.

RÉSUMÉ

Les injections de moyen de contraste dans l'aorte et dans la carotide chez les sujets atteints probablement de mort cérébrale avec ou sans arrythmie ont provoqué une baisse importante de la pression sanguine systémique; ceci dépendait de la présence ou de l'absence d'une circulation sous-tentorielle. L'angiographie vertébrale n'entraînait pas de diminution de la pression sanguine systémique et peut donc être recommandée pour la détection d'un arrêt complet de la circulation cérébrale.

REFERENCES

- BOKOVIC N. Stagnant anoxia and carbon monoxid poisoning. *Electroenceph. clin. Neurophysiol.* (1963) Suppl. No. 21, p. 11.
- BUCHHEIM E., KAUFER C. und DUX A. Zerebrale Angiographie zur Bestimmung des Hirntodes. *Fortschr. Röntgenstr.* 113 (1970) 278.
- FISCHER H. W. and FOLSTEIN J. W. Comparison of cerebral angiographic contrast media by the circulatory effects. *Amer. J. Roentgenol.* 86 (1961) 106.
- GRITZ T. A radiologic study of the brain circulation by rapid acrial angiography of the carotid artery. *Acta radiol.* (1956) Suppl. No. 140.
- HENRIKSEN O. Cerebral circulatory arrest caused by acute increase of intracranial pressure. A clinical and roentgenological study of 25 cases. *Acta neurol. scand.* (1964) Suppl. No. 7.
- HITAL S. Hemodynamic changes associated with the intraarterial injection of contrast media. *Radiology* 86 (1969) 615.
- JØRGENSEN E. O. EEG as related to arteriography and neurological findings in patients with fatal traumatic brain damage, brain tumours and cerebral vascular disease. Annual report. *Inst. Neurophysiol. University of Copenhagen*, p. 25. Unpublished, Copenhagen 1971.
- and BRODERS P. Criteria of death. *Nord. Med.* 86 (1971) 1549.
- LUNDQVIST P. The mesencephalon and the vasomotor system. *Acta physiol. scand.* (1955) Suppl. No. 121.
- and TORILL G. Blood pressure and heart rate responses in carotid angiography with sodium acetate. *Acta radiol.* 50 (1958) 160.
- LUNDQVIST A. and EGGSTEDT A. Electroencephalographic and electrocardiographic studies of complications in cerebral angiography. *Acta radiol. Diagnosis* 9 (1969) 199.
- MITCHELL O. C., DE LA TORRE E., ALEXANDER E. and DAVIS C. H. The nonfilling phenomenon during angiography in acute intracranial hypertension. *J. Neurosurg.* 19 (1962) 768.
- SELDINGER S. I. Catheter replacement of the needle in percutaneous arteriography. *Acta radiol.* 39 (1953) 368.
- VLADOVITZ B., FERREREAU P., KUHNER A., BILLET M. et GROS C. Les angiographies sous pression dans la mort du cerveau avec arrêt circulatoire cérébral. *Neurochirurgie* 17 (1971) 81.
- ZEMEK Z., GERGELY R. und GERGELY M. Experimentell. Untersuchungen bei der Angiokardiographie. *Fortschr. Röntgenstr.* 81 (1954) 9.
- ZWETKOV N. N. Effects on increased cerebrospinal fluid pressure on the blood flow and on the energy metabolism of the brain. *Acta physiol. scand.* (1970) Suppl. No. 339.

DESCENT OF CEREBROSPINAL FLUID TO SPINAL SUBARACHNOID SPACE

G DI CHIRO S M LARSON T HARRINGTON G S JOHNSTON M V GREEN
and SYBIL J SWANN

Scintigraphy has been used extensively to investigate the bulk flow of the cerebrospinal fluid (CSF) in human beings (DI CHIRO & ASHBURN 1971 DI CHIRO et coll 1964 HARBERT et coll 1972 KIEFFER et coll 1971).

External scintillation scans of the head performed at various time intervals after the intraventricular or intrathecal introduction of different isotopes have proven beyond any doubt the existence of an active ascending transport of the injected tracer toward the hemispheric cerebral convexities (DI CHIRO 1964 1966). The descending path of the CSF to the spinal subarachnoid space on the other hand has been only briefly commented upon mostly in reference to isotope ventriculography in abnormal conditions (DI CHIRO 1966 LARSON et coll 1972 MINOMAR & HAMMOCK 1971). This report deals with the downward progression in the spinal subarachnoid space of isotopes injected into the ventricular system or the basal cisterns of normal Rhesus monkeys.

Material and Methods Fourteen Rhesus monkeys weighing between 2.5 and 5 kg were used. The animals were anesthetized and an isotope was introduced



Fig. 1



Fig. 2a



Fig. 2b

Fig. 1 Rapid downward flow of tracer injected into lateral ventricle. Dark outline of monkey head obtained by transmission scanning.

Fig. 2 a) Isotope injected within lateral ventricle (top arrow) quickly reaches fourth ventricle (bottom arrow) and then posterior cervical subarachnoid space. b) Two minutes later activity is seen in front of brain stem (arrow). Transmission scanning of head outline.

(slowly and without barbotage in an attempt to avoid a flushing effect) into the cerebrospinal fluid spaces by one of the following routes: (1) through a twist drill hole into one lateral ventricle — six monkeys; (2) by a suboccipital puncture into the cisterna magna — four monkeys; (3) through a twist drill hole into the basal cisterns in front of the brain stem — two monkeys; (4) both into one lateral ventricle and the cisterna magna — two monkeys. Two human serum albumin (HSA) tracers of different gamma energies, ^{125}I HSA (100 μCi) and $^{99\text{m}}\text{Tc}$ HSA (1 mCi) (Di Chiara et coll. 1968) were used separately or in combination for the various injections. The commercial preparation of ^{125}I HSA contained no detectable free ^{125}I iodide. $^{99\text{m}}\text{Tc}$ HSA was prepared at our institution (National Institutes of Health) and it contained less than 2 per cent unbound $^{99\text{m}}\text{TcO}_4^-$.

Immediately after the introduction of the isotope sequential scans of the head and spine in the anterior, posterior and both lateral projections were obtained using an Anger type scintillation camera fitted with a pin hole collimator of 4.0 mm diameter. Scans were taken for one to seven hours after the injection. The temporal spacing of the sequential images was very close (each few seconds and at times as fast as the rapid serial Polaroid views could be obtained) in the first minutes while later in the experiment, scans were separated by longer times (up to fifteen minutes).

In four of the monkeys in which an intraventricular injection of ^{125}I HSA had been carried out digital analysis of the movement of the tracer was performed using a small dedicated computer (HP 5407A Hewlett Packard Scintigraphic



Fig 3 Fifteen minute scan shows descent of isotope into spinal subarachnoid space Outline of monkey head neck and chest by transmission camera

Data Analyzer) mated to the Anger camera. For this purpose the pin hole collimator was positioned so that the entire lateral length of the cerebrospinal fluid space was within the field of view of the Anger camera detector. Nine regions of interest cursors were drawn along the entire length of the spinal cord. The cursors were contiguous but did not overlap. Two additional cursors were drawn on over the cerebral convexities and one to include the entire spinal subarachnoid space. Time activity curves were then obtained from each region of interest simultaneously without moving the animal for the next three and one half hours.

Results

The ventricular system communicates with the subarachnoid space through three foramina of the fourth ventricle: the median inferior aperture of Magendie which opens into the anterior section of the cisterna magna (vallecula) and the lateral apertures of Luschka (lateral recesses) which communicate with the lateral parts of the medullary cistern and the pontocerebellar cisterns. We have verified by anatomic dissections that this arrangement present in man (MILLEN & WOOLLAM 1962) is also found in the Rhesus monkey.

The isotope injected within the lateral ventricles of the Rhesus monkey flows very rapidly into the third and fourth and out of the ventricles (Fig 1). In the one minute scan the tracer is seen passing straight down through the foramen of Magendie into the cisterna magna and the upper posterior cervical segment of the subarachnoid space (Fig 2 a). Soon after (2—3 minutes) we observe the lateral passage through the apertures of Luschka into the medullary and ponto-

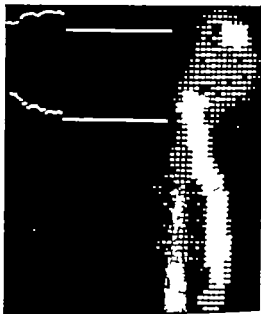


FIG. 4. Time-lapse activity curves (left of base-lines) of two cursors, one over cerebral convexity (top) and one over upper cervical segment (bottom). Curves, which have been initiated about one hour after ventricular introduction of isotope show progressive decrease of spinal activity during seven hours. Concomitantly activity over brain convexity increases.

cerebellar cisterns and from here anteriorly toward the pontine and mid-penduncular cisterns (Fig. 2 b). Later (15 minutes to 2—3 hours) the scans demonstrate both the spinal descent (Fig. 3) and the ascent toward the Sylvian fissures and the convexity of the brain.

The analysis of the time-activity curves from several regions of interest over the CSF cavities after the endoventricular introduction of the isotope confirms the progression of the activity in both directions, descending and ascending. With time an equilibrium of the activity within the spinal subarachnoid space is reached. In the cervical and upper thoracic segments, the rate of clearance of the isotope progressively diminishes with movement down the spine. In the mid-thoracic area there is a region of balance between incoming and outgoing activity so that the time-activity curve (and presumably concentration) maintains a constant level. Below this point in the lower thoracic and upper lumbar area, the concentration constantly increases during the investigation. In the later (several up to seven hours) spinal scans the total activity progressively decreases. During this time the cursor over the cerebral convexity near the superior longitudinal scans, clearly shows a progressive increase in cerebral subarachnoid space activity (Fig. 4).

When the isotope is introduced within the cisterna magna, the descending movement toward the spine is even more marked and in the later (five to seven

hours) scans high activity is still present in the lower spinal segments with no significant activity diminution. This is also confirmed by our double tracer examinations with injection of $^{99}\text{Tc}^m$ HSA within the ventricular system and ^{125}I HSA into the cisterna magna. If the isotope is injected into the basal cisterns in front of the brain stem the tracer moves in a prevalent ascendant direction toward the convexity of the brain.

We have also observed that initially, regardless of the site of injection (endoventricular or external) the isotope descends in the posterior part of the upper cervical subarachnoid space at an early stage while later and lower down in the spine no such streaming in the posterior or anterior parts of the spinal subarachnoid space is evident. On the basis of some anatomic observations on the spinal CSF cavities (DI CUNEO & FISCHER 1964) we had postulated (DI CUNEO 1966) the existence of double currents within the spinal subarachnoid space: one prevalently descending behind and one ascending in front of the denticulate ligaments. The present investigation gives only partial support to this theory. No attempt has been made to appraise the fluid movement within the central canal of the spinal cord.

One of the monkeys was killed immediately after intrathecal injection of ^{125}I HSA into the cisterna magna and time activity curves were obtained over the spine after death in a fashion similar to that used for the living animals. In the dead monkey no passage of activity below the upper cervical cord was found during the next five hours after injections.

The transport phenomena described above apply to albumin tagged tracers which are entrained in the CSF bulk flow. It is uncertain whether smaller molecular weight compounds move in a similar fashion within the CSF cavities since here fluid and tissue diffusional transport may play a bigger role. In a previous investigation (DI CUNEO 1964) we noted that a compound with molecular weight of 163 ($^{99}\text{Tc}^m\text{O}_4^-$) injected intraventricularly failed to be transported with the cerebrospinal fluid and it was mainly resorbed at and around the site of injection.

SUMMARY

Albumin tagged with gamma emitting isotopes injected into the lateral ventricles of the Rhesus monkey brain flows rapidly into the spinal subarachnoid space. This is followed first by equilibration and later by decrease of spinal activity as well as concomitant augmentation of cerebral convexity subarachnoid activity. When the isotope is introduced via the cisterna magna, the observed spinal descent is even more marked whereas an injection into the anterior basal cisterns is followed by a prevalent ascent of the tagged albumin toward the convexity of the brain.

probably depends not only on the adhesiveness of the platelets *per se* but also on the tendency of the catheter material to elicit the adhesion of the platelets.

Most methods available for measuring the thrombogenic properties of a material reflect only the physical and chemical properties of the latter or its effect on coagulation (LYMAN *et al.* 1965; GOTT 1966). The degree of platelet adhesion and aggregation with different materials *in vitro* may constitute a better measure for this purpose than those hitherto used.

The intention of the present investigation was first, to devise a method for quantifying the adhesion of platelets to catheter materials *in vitro* after the rotation of citrated blood in catheter hoops and, secondly, to ascertain whether the method could be used for appraising the tendency of a given material to initiate thrombus formation.

Set up and procedures

Citrated blood was poured into vascular catheters 1 meter long and 1.8 mm in inner diameter, i.e. with a volume of about 2.5 cm³. The ends of each catheter were joined by an outer plastic muff, after which the catheters were mounted around a 10 cm high cylinder. The cylinder was fastened to a turntable which sloped at an angle of about 35° and could be rotated at a rate of 4 rpm (Fig. 1). On rotation of the table the blood spread over the entire surface of the catheter. In each experiment 1 ml of citrated blood was poured into each catheter, which was allowed to rotate for 1 hour—except in those experiments in which the effect of the blood volume and contact time were examined. The catheters were emptied after the experiments by allowing the blood to run down into a test tube.

Analysis and calculations. Platelet retention to the catheters, i.e. adhesion or aggregation or both, will be referred to as platelet adhesiveness or simply as adhesion.

The platelets remaining in each catheter were expressed relative to the amounts added, according to the formula:

$$\text{Adhesion (\%)} = 100 \times \frac{\text{prerotational count} - \text{postrotational count}}{\text{prerotational count}}$$

With labelled platelets, activity/g was used instead of the count. The calculation thus measured the capacity of the individual catheters to 'clear' a certain amount of citrated blood of platelets.

Laboratory methods. The isotope labelling of dog platelets was done *in vitro* with ⁵¹Cr (250 μCi) by the FOSS ABRAHAMSEN (1968) modification of the method of AAS & GARDNER (1958). Labelling was performed at least one day



Fig. 1 Set up used in estimation of adhesion of platelets to vascular catheters

before sampling. The radiation activities were measured with a 7.6 cm NaI well crystal (Autowell II Picker). If the activity in 1 ml of whole blood 24 hours after the labelling were less than about 800 counts/min the animal was rejected.

Blood samples both in the dog and human subject were collected in 10 ml siliconed tubes containing 1 ml of 3.8% trisodium citrate solution ($\text{Na}_2\text{C}_6\text{H}_5\text{O}_7 \times 2\text{H}_2\text{O}$)—except in those experiments in which the significance of the amount of citrate added was investigated. The blood was poured into the catheters about 15 minutes after collection—except when storage was examined for its effect on adhesiveness.

The haematocrit was determined in duplicate microhaematocrit tubes. The result was not corrected for dilution because the values obtained were utilized only for the comparison of one and the same sample before and after the procedure.

Platelet poor plasma was prepared by spinning blood samples in a MSE Super Multex centrifuge for 20 minutes at 2 000 g and afterwards pipetting off the plasma. The platelets were counted by Björckman's (1959) method but without the addition of EDTA.

Experimental and Results

Testing of the method

Only labelled dog platelets with polyethylene (PE 260 Intramedic Clay Adams) as a catheter compound were used for testing the method. All the ex-

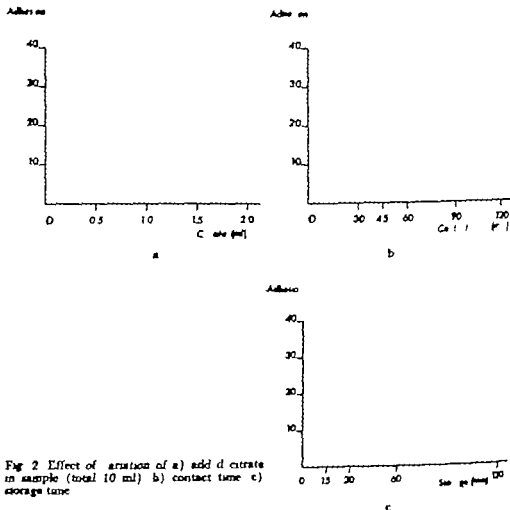


Fig. 2. Effect of variation of a) added citrate in sample (total 10 ml) b) contact time c) storage time.

periments were carried out at room temperature. Adhesion was calculated from the means of three parallel determinations. Each variable mentioned below was analysed only once per dog, and the values given are the means of determinations in 4 animals. These results were not treated statistically.

Citrate content. Venous blood samples were obtained in 10 ml tubes containing 2, 1.5, 1 or 0.5 ml citrate solution. The adhesiveness of the platelets in the various samples was determined and proved to vary inversely with the amount of citrate solution added (Fig. 2 a) the amount could be reduced only to 1/10 as otherwise the blood coagulated.

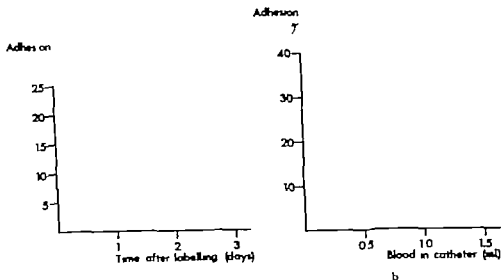


Fig 3 Effect of a) interval after labelling b) blood volume in catheter on adhesion of platelets

Contact time The adhesion was examined after 15 30 60 90 and 120 minutes rotation. The values increased up to 60 minutes contact time after which they remained stationary (Fig 2 b)

Storage time For technical reasons a regular delay of about 15 minutes occurred between sampling (in the animal stable) and analysis (at the laboratory). Further storage of the samples for 15 45 and 100 minutes was undertaken for any effect on adhesiveness: no such effect was apparent (Fig 2 c)

Age of platelets The adhesiveness was examined on the 1st, 2nd and 3rd day after labelling. The values tended to be lower on the third day (Fig 3 a)

Amount of blood added Volumes of 0.5 1.0 and 1.5 ml citrated blood were compared for differences in adhesion to the catheters. The adhesiveness fell with increasing amount of blood in the catheter (Fig 3 b) suggesting that the remnants of platelets in the catheters were relatively constant regardless of the amount of blood poured into the catheter.

Haematocrit and radioactivity in platelet poor plasma were measured before and after contact of the blood with the catheters. No differences were evident

Emptying of catheter After contact with the catheter the blood was drawn off in three separate portions of relatively different sizes and the adhesion calculated from the respective samples. No differences between the values were obtained.

Adhesiveness of platelets not retained Blood that had been rotated for one hour was transferred to further catheters and rotated for a further hour. The adhesion after contact with one catheter was calculated as 24 per cent and after contact with a fresh surface for another hour as 46 per cent.

Precision of the method

The above findings suggested an examination of vascular catheters of the above dimensions with 1 ml of blood containing 1/10 citrate. The tests were started about 15 minutes after the collection of the blood and one hour was chosen as the contact time. These conditions were also considered acceptable when the adhesion was calculated from unlabelled platelet counts. The adhesion of ^{51}Cr labelled platelets was examined only on the first 2 days after the day of labelling.

The precision of the method for measuring platelet adhesion was calculated from 18 triple determinations in samples from 9 dogs and 9 human volunteers. When ^{51}Cr labelled dog platelets were used the standard deviation was 3.8 with corresponding determinations calculated from dog and human platelet counts the values became 4.06 and 3.28 respectively.

Examination of catheter materials

The experiments were carried out with the above method and the following catheter compounds investigated: polyethylene (Intramedic, Clay Adams), polyethylene with lead oxide (Ödman-Ledum, KIFA) and teflon (Du Pont).

All catheters had the dimensions mentioned.

The experiments were carried out in three series: I — 9 dogs, platelets labelled with ^{51}Cr ; II — 9 dogs with unlabelled platelets; III — 12 healthy human volunteers.

The adhesion to the respective materials was calculated from the mean of three parallel determinations. In series I the platelet content in the samples was estimated from the activity of the isotopes—in series II and III from platelet counts. Comparisons were made between pairs of observations by comparing the means of paired differences by Student's *t* test at the significance level of 0.05.

The results revealed that the materials could be ranked with respect to adhesion of platelets (Table). Statistical analysis demonstrated that the adhesion

Table

Adhesion (per cent) of labelled and unlabelled platelets to different vascular catheter materials n = number of experiments

	Cr dog platelets (n = 5)	Dog platelets (n = 5)	Human platelets (n = 12)
Polyethylene with lead oxide	32	35	47
Polyethylene	23	27	42
Teflon	13	18	38

to the polyethylene with lead oxide catheter was significantly greatest and that to the teflon catheter least. The ranks of the individual materials were the same whether the experiments were carried out with labelled or unlabelled dog platelets. Human platelets also reacted in the same way to the various materials.

Discussion

The testing of the method indicated that the adhesion of labelled platelets to vascular catheter materials may be calculated from the difference in radioactivity of a blood sample before and after its contact with a given catheter surface. The finding that the haematocrit remained unchanged after such contact and that the concentration of ^{51}Cr did not vary with the size of various aliquots tapped from the catheter after rotation meant that the retention of platelets was not due to sedimentation but to adhesion.

It was decided to use labelled platelets for the testing of the method because such platelets adhere to vascular catheter materials (JACOBSSON) and further because isotope counting measures the entire amount of platelets irrespective of their condition. Since a varying proportion of the platelets that have been in contact with the catheter are aggregated (JACOBSSON) the use of an isotope was thought to be a more reliable method for calculating the total amount of platelets adherent to the catheter wall.

The platelets were never examined for adhesion on the day they were labelled, because soon after labelling some of the radioactivity may be due to elution of

Cr from the platelets (EMER et al. 1965). Nor were examinations performed more than two days after the labelling because of the decrease in their adhesiveness (Fig. 3a). The decrease on the third day corroborates the observations of WRIGHT (1941) and HUBB et al. (1968) that young platelets are more adhesive than older ones.

Implying of catheter After contact with the catheter the blood was drawn off in three separate portions of relatively different sizes and the adhesion calculated from the respective samples. No differences between the values were obtained.

Adhesiveness of platelets not retained Blood that had been rotated for one hour was transferred to further catheters and rotated for a further hour. The adhesion after contact with one catheter was calculated as 24 per cent and after contact with a fresh surface for another hour as 16 per cent.

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The precision of the method for measuring platelet adhesion was calculated from 18 triple determinations in samples from 9 dogs and 9 human volunteers. When ^{51}Cr labelled dog platelets were used the standard deviation was 3.78 with corresponding determinations calculated from dog and human platelet counts the values became 4.06 and 3.28 respectively.

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The adhesion to the respective materials was calculated from the mean of three parallel determinations. In series I the platelet content in the samples was estimated from the activity of the isotopes—in series II and III from platelet counts. Comparisons were made between pairs of observations by comparing the means of paired differences by Student's *t* test at the significance level of 0.05.

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The platelets were never examined for adhesion on the day they were labelled because soon after labelling some of the radioactivity may be due to elution of

Cr from the platelets (ENGE et coll 1965). Nor were examinations performed more than two days after the labelling because of the decrease in their adhesiveness (Fig 3 a). The decrease on the third day corroborates the observations of WUJOWITZ (1941) and HUGHES et coll (1968) that young platelets are more adhesive than older ones.

Though adhesion diminished inversely with the amount of blood poured into the catheter (Fig. 3b) it was nevertheless decided to use 1 ml of citrated blood throughout: this was a volume considered large enough to avoid an unreasonable large error of the single observation and at the same time not so large as to impair its flow during rotation of the catheter.

The finding that adhesion, within certain limits, increased with the contact period corroborates the observations made previously by HALLÉN (1960) and by WRIGHT. The variation of adhesion with contact time has also been emphasized by CROWBERG (1967).

The experiments in which blood that had been rotated for one hour was transferred to other catheters and rotated again for another hour like those in which different amounts of blood were poured into the catheters, indicated the reason why adhesion reached a maximum after a certain time. This was not depletion of platelets in the blood samples but saturation of the surface of the catheter.

It would appear that the thrombogenic properties of a material may be adequately defined as its tendency to initiate thrombus formation since it is only the initial step of thrombosis that may with certainty be ascribed to the foreign material while the further course and final fate of thrombi formed depends on other factors. Comparison of different catheter materials regarding adhesion of platelets offers a possibility of investigating the role played by a given material in the provocation of the initial steps of thrombus formation. Platelet adhesion thus seems to be a well founded measure of the thrombogenic quality of a given material.

The examination of the materials confirmed that the method devised is suitable for comparing the thrombogenic properties of different catheter materials. The tests indicate that polyethylene with lead oxide was the most and teflon the least thrombogenic. The ranks of the materials were the same whether judged from the measurement of ^{51}Cr activity or platelet counts. Both methods may thus be used for testing materials. Though no further attempts were made to compare the two methods for calculating platelet adhesiveness, the results suggested that the differences between them were only quantitative.

The results of the above experiments in dogs and human subjects agree not only with one another but also with corresponding observations made *in vivo* (SCHLOSSMAN). It is therefore most probable that the *in vitro* method reflects what really happens *in vivo* in man. This therefore suggests that it may be used with advantage and to some extent even replace testing of materials *in vivo*.

Acknowledgement

This investigation was supported by grants from the Swedish Medical Research Council and the Swedish Cancer Society.

SUMMARY

A method is described for quantitative comparison of the adhesion of platelets of the blood to vascular catheter materials in vitro. Three materials, i.e. teflon, polyethylene and polyethylene with lead oxide with such adhesion as measure of their thrombogenic properties were compared. The adhesion was calculated from measurements of the radioactivity of labelled dog platelets and counts of unlabelled dog and human platelets.

ZUSAMMENFASSUNG

Eine in vitro-Methode zum quantitativen Vergleich der Adhäsion von Blut Thrombozyten an erprobtes Material für vasculäre Katheter wird beschrieben. Drei verschiedene Substanzen Teflon Polyäthylen und Polyäthylen mit Bleioxyd wurden mit dieser Adhäsionsmethode hinsichtlich ihrer Thrombosehervorrufenden Eigenschaften untersucht. Die Adhäsion wurde durch Radioaktivitätsmessungen gezeichneter Hund-thrombozyten und Messungen ungezeichneter Thrombozyten vom Hund und Menschen bestimmt.

RÉSUMÉ

Les auteurs décrivent une méthode de comparaison quantitative de l'adhérence des plaquettes du sang aux matériaux de cathéter vasculaire in vitro. Trois matériaux, le téflon, le polyéthylène et le polyéthylène avec oxyde de plomb ont été comparés en étudiant cette adhérence des plaquettes comme mesure de leurs propriétés thrombogènes. L'adhérence des plaquettes a été calculée à partir de mesure d'radio-activité de plaquettes marquées de chiens et à partir de numération de plaquettes non marquées de chiens et de sujets humains.

REFERENCES

- AAS H. A. and GARDNER F. H. Survival of blood platelets labelled with chromium 51. *J. clin. Invest.* 37 (1958) 1257.
- BJORSEMAN S. E. A new method for enumeration of platelets. *Acta haemat. (Basel)* 22 (1959) 377.
- CRONBERG S. Methodological problems in testing of platelet adhesiveness. *Scand. J. Haemat.* 4 (1967) 385.
- EMER S., BAUDON M. and DONOVAN J. Comparative studies of platelet survival by different methods in the rabbit. *Blood* 25 (1965) 548.
- EVANS G. and IRVING W. T. Long term arterial graft patency in relation to platelet adhesiveness, biochemical factors and anticoagulant therapy. *Lancet* 1966 II p. 333.
- FOUR ABRAHAMSEN A. A modification of the technique for ^{51}Cr labelling of blood platelets giving increased circulating platelet radioactivity. *Scand. J. Haemat.* 5 (1968) 53.
- GLYNN M. F., MURPHY E. A. and MINTHAU J. F. Platelets and thrombosis. *Ann. intern. Med.* 64 (1966) 715.
- GOTT V. L. The causes and prevention of thrombosis on prosthetic materials. *J. surg. Res.* 6 (1966) 274.
- HAMPSON J. R. The study of platelet behaviour and its relevance to thrombosis. *J. Atheroscler. Res.* 7 (1967) 29.
- HELLER A. J. The adhesiveness of human blood platelets in vitro. *Scand. J. clin. Lab. Invest.* (1960) Suppl. No. 51.

- HIRSCH J, GUYON M F and MUSTARD J F The effect of platelet age on platelet adherence to collagen *J clin Invest* 47 (1968) 466
- JACOBSSON B Platelet adhesion and aggregation following contact between blood and vascular catheters in vitro *Scand J Haemat* 6 (1969) 216
- LYMAN D J, MUIR W M and LEE I J The effect of chemical structure and surface properties of polymers on the coagulation of blood. I. Surface free energy effects *Trans Amer Soc artif intern Organs* 11 (1965) 301
- MUSTARD J F, MURPHY E A, ROWELL H C and DOWNEY H G Factors influencing thrombus formation *Amer J Med* 33 (1962) 621
- and PACKHAM M A Thromboembolism: A manifestation of the response of blood to injury *Circulation* 42 (1970) 1
- SCHLOSSMAN D Thrombogenicity of vascular catheter materials in vivo: The difference between materials *Acta radiol Diagnost* 14 (1973) 97
- WRIGHT H P The adhesiveness of blood platelets in normal subjects with varying concentrations of anticoagulants *J Path Bact* 53 (1941) 255

CONTRAST FORMATION IN FLUOROSCOPIC VIDEODENSITOMETRY

I A mathematical model for optimising contrast in radiography

K.-G. STRID and B. LANTZ

The development of roentgen videodensitometry at the Mayo Clinic by STURM et coll (1964) and application of this method to a quantitative analysis of blood flow within central and peripheral circulation has attracted more and more interest since the end of the 1960s (WOOD et coll 1964 OTTFKA & HEINTZEN 1967 RUTISHAUSER 1967 RUTISHAUSER et coll 1967 SILVERMAN 1970 WOOD & STURM 1970 HEINTZEN 1971). The method consists of measuring small absorption changes caused by an iodine contrast medium in a selected area of the object. During the past several years extensive investigations have been carried out in this roentgen department to establish the parameters determining the behaviour of a contrast medium in pulsative flow (LANTZ 1973). In those investigations we have used a well balanced detector system in which the densitometric unit contains a specially constructed window generator the output signal of which is made logarithmic for linearity (Fig 1). The measurements have been made from a small area of a television image recorded on tape in television fluoroscopy with fixed tube voltage and current

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- HIRSCH J, GLYNN M F and MUSTARD J F The effect of platelet age on platelet adherence to collagen *J clin Invest* 47 (1968) 466
- JACOBSSON B Platelet adhesion and aggregation following contact between blood and vascular catheters in vitro *Scand J Haemat* 6 (1969) 216
- LYMAN D J, MITT W M and LEE I J The effect of chemical structure and surface properties of polymers on the coagulation of blood. I. Surface free energy effects *Trans Amer Soc artif intern Organs* 11 (1965) 301
- MUSTARD J F, MURPHY E A, ROWELL H C and DOWNTON H G Factors influencing thrombus formation *Amer J Med* 33 (1962) 621
- and PACKHAM M A Thromboembolism: A manifestation of the response of blood to injury *Circulation* 42 (1970) 1
- SCHLOSSMAN D Thrombogenicity of vascular catheter materials in vivo: The difference between materials *Acta radiol Diagnosis* 14 (1973) 97
- WRIGHT H P The adhesiveness of blood platelets in normal subjects with varying concentrations of anticoagulants *J Path Bact* 53 (1941) 255

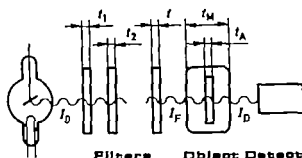


Fig. 2 Radiographic system

Contrast formation

In a radiographic system (Fig. 2) a roentgen source delivers radiation of which the spectral distribution with respect to frequency ν is $I_\nu = dI/d\nu$; I being the total radiation intensity. The radiation is filtered by a number of absorbing sheets of thickness t_1, t_2, \dots, t and frequency dependent linear extinction coefficient $\mu(\nu), \mu(\nu), \dots, \mu(\nu)$. After filtering the radiation has the spectral intensity distribution

$$I_F(\nu) = I(\nu) \exp \left[- \sum_{i=1}^n \mu_i(\nu) t_i \right] \quad (1)$$

The radiation then has to pass the object under investigation before reaching the detector. In angiography the object is suitably considered as a homogeneous body of thickness t_M and linear extinction coefficient $\mu_M(\nu)$ in which a contrast substance can be introduced into a layer of thickness t_A giving this layer the additional linear extinction coefficient $\mu_A(\nu)$. The spectral intensity distribution of the radiation reaching the detector is then

$$I_D(\nu) = I_F(\nu) \exp \left[- \mu_M(\nu) t_M - \mu_A(\nu) t_A \right] \quad (2)$$

The detector responds to this radiation with a signal S (e.g. blackening of photographic material, output voltage from a photoelectric device) which depends on the weighted total intensity reaching it

$$S = f(J) \quad (3)$$

$$J = \int s(\nu) I_D(\nu) d\nu \quad (4)$$

$s(\nu)$ being the spectral sensitivity of the detector. Obviously J and thus S vary with varying μ_A .

In angiography the extinction coefficient μ_A depends on the concentration C_A of contrast medium in the contrasting layer. One may define a contrast function

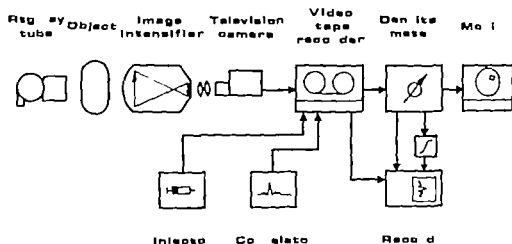


Fig. 1. Block diagram of radiodensitometric system for blood flow measurement.

If quantitative densitometry is to be based on absorption of the radiation by a contrast medium, two further factors have to be taken into consideration in addition to the detector system, namely the radiation source and the absorption process. The present paper describes a method of computing the contrast in radiography in order to optimize it. The results thus computed will be tested by using a linear detector system. Furthermore, the validity of the Lambert Beer law, i.e. that the extinction be a linear function of the amount of contrast substance, will be tested within the range of clinical interest.

In order that high contrast be obtained in radiography, the absorption of the radiation in differing parts of the object should be as different as possible. The absorption of the rays is not only dependent on the object but also strongly on the wavelength. Thus the contrast is influenced by the spectral distribution of energy in the radiation. It is well known that the hardness of the radiation determines the contrast in radiography.

In Part I a mathematical model of the contrast formation is given, including the emission from the tube target, the absorption process and the conversion of the absorption relief into an image. The discussion mainly concerns the contrast formation in angiography but may easily be extended to any kind of radiography.

In Part II (LANTZ & STRID 1973) the computed contrast data will be compared with experimentally measured values.

$$\lambda_{\max} \approx \frac{3}{2} \lambda_0 \frac{1}{1 + (b/c)\lambda^2}$$

Usually the last term in (6) or (8) can be neglected i.e. $b\lambda^2 \ll c$ and then

$$\lambda_{\max} = \frac{3}{2} \lambda_0$$

DAUVILLIER (1920) found experimentally that $\lambda_{\max}/\lambda_0 \approx 1.3$ whereas KULEN KAMPTZ (1922) obtained $\lambda_{\max}/\lambda_0 \approx 1.28-1.48$ for various metals.

For the purpose of contrast calculations we will put $b = 0$.

Characteristic spectrum The characteristic x-ray emission spectrum of an element consists of lines belonging to the K, L, M, \dots series. A certain series say E , is excited when the accelerating voltage, U_0 , exceeds a characteristic value U_E related to the corresponding absorption edge frequency ν_E :

$$qU_0 = h\nu_E \quad (9)$$

According to WEBSTER (1927) the number N_E of emitted E line photons is proportional to the number N_B of continuum photons emitted with frequency between the E excitation frequency ν_E and the cut off frequency ν_0 ,

$$N_E = Q_E \lambda_B, \quad (10)$$

where

$$\lambda_B = \int_{\nu_E}^{\nu_0} \frac{I(\nu) d\nu}{h\nu}$$

assuming the intensity I to be equal to the radiation energy Q being a constant, w_E being the probability that the excited electron returns to a E level and $h\nu_E$ being the energy of a photon of frequency ν . WEBSTER found experimentally that Q does not depend on U . For silver he determined $Q = 0.96$.

For the present purpose an exact description of the spectrum is not required, and it then seems reasonable to put $Q_{E\lambda} \approx 1$. Moreover equation (10) is extended to an arbitrary series E by putting

$$\lambda_E = \int_{\nu_E}^{\nu_0} \frac{I(\nu) d\nu}{h\nu} \quad (11)$$

The series of importance in clinical radiography are the K and L series. The most prominent lines of the K series are the $K\alpha_1, K\alpha, K\beta_1$ and $K\beta_2$, with relative intensity values 100, 50, 30, 15 (cf. REGLER 1937 p. 19) which has been established both experimentally and by quantum mechanical calculations. The strongest L lines are the $L\alpha_1, L\alpha, L\beta$ and $L\beta_2$ with the approximate intensity ratio 100, 10, 50, 20 (cf. REGLER 1937 pp. 20-22). Since the

$$I_h = \frac{U}{100} (U - U_h) \quad (20)$$

where $U_h = (h - \frac{1}{2}) U_0/100$ corresponds to the energy in the centre of that interval. For the characteristic lines the intensity is calculated from (12) as

$$\left. \begin{aligned} I_{K\alpha} &= \frac{10}{19} U_{hK\alpha} \left(U \ln \frac{U}{U_A} + U + U_A \right) \\ I_{h\beta} &= \frac{9}{13} U_{h\beta} \left(U \ln \frac{U}{U_A} - U + U_A \right) \\ I_L &= U_{L\alpha} \left(U \ln \frac{U}{U_{LIII}} - U + U_{LIII} \right) \end{aligned} \right\} \quad (21)$$

respectively U_A and U_{LIII} being the excitation voltage values for the K and L_{III} levels respectively and $qU_{hK\alpha}$, $qU_{h\beta}$ and $qU_{L\alpha}$ being the photon energy values of $K\alpha$, $h\beta_1$ and $L\alpha$ radiation respectively. The total intensity emitted by the anticathode is obtained as

$$T_A = \sum_{h=1}^{100} I_h + I_{K\alpha} + I_{h\beta} + I_L \quad (22)$$

The distribution of energy received by the detector. The intensity of radiation reaching the detector is reduced by absorption in materials inserted between the anticathode and the detector. For each absorbing atomic species the extinction coefficient is given by (17). For an absorbing species of thickness t_j the extinction for photons of energy qU is conveniently expressed as

$$\tau_j(U) t_j = \pi_j \frac{\Delta f_j(U)}{U} \quad (23)$$

where

$$\pi_j = \left[2r \frac{hc}{q} N \right] \frac{qf}{Vf_j} t_j \quad (24)$$

is a constant relating to the atomic species j the wavelength has been expressed as

$$\lambda = \frac{hc}{qU} \quad (25)$$

h being Planck's constant. The constant in brackets in (24) is evaluated as

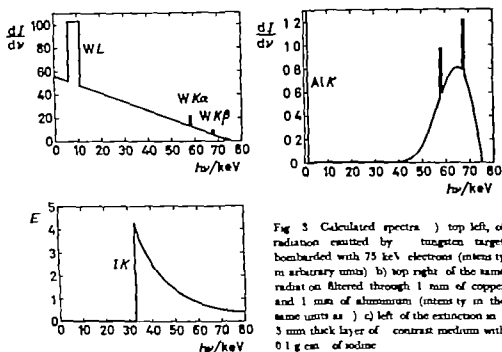


Fig 3 Calculated spectra a) top left, of radiation emitted by tungsten target bombarded with 75 keV electrons (intensity in arbitrary units) b) top right of the same radiation filtered through 1 mm of copper and 1 mm of aluminum (intensity in the same units as a) c) left of the extinction in 3 mm thick layer of contrast medium with 0.1 g/cm² of sodium

$$2r \frac{hc}{q} \lambda = 1.081 \times 10^{-8} \text{ m kmol}^{-1} = 1.081 \times 10^{-8} \text{ cm mol}^{-1}$$

Δf_j (U) is calculated from (15) and (16). According to (2c)

$$P_{aj} = \frac{P_a hc}{q} \times \frac{1}{U}$$

where

$$\frac{R_a hc}{q} = 13.61 \text{ V} = 1.361 \times 10^{-4} \text{ kV}$$

If diffuse scattering is neglected the total extinction is

$$E(U) = \frac{1}{U} \sum_j a_j \Delta f_j(U) \quad (26)$$

The intensity of radiation of the k th energy interval reaching the detector is then

$$I_{Da} = I_a \exp[-E(U_k)] \quad (27)$$

and the total intensity received by the detector is

$$I_k = \frac{U}{100} (U - U_k) \quad (20)$$

where $U_k = (k - \frac{1}{2}) U / 100$ corresponds to the energy in the centre of that interval. For the characteristic lines the intensity is calculated from (12) as

$$\left. \begin{aligned} I_{K\alpha} &= \frac{10}{13} U_{K\alpha} \left(U \ln \frac{U}{U_K} + U + U_K \right) \\ I_{K\beta} &= \frac{3}{13} U_{K\beta} \left(U \ln \frac{U}{U_K} - U + U_K \right) \\ I_L &= U_{L\alpha} \left(U \ln \frac{U}{U_{LIII}} - U + U_{LIII} \right) \end{aligned} \right\} \quad (21)$$

respectively U_K and U_{LIII} being the excitation voltage values for the K and L_{III} levels, respectively, and $qU_{K\alpha}$, $qU_{K\beta}$ and $qU_{L\alpha}$ being the photon energy values of $K\alpha$, $K\beta$ and $L\alpha$ radiation respectively. The total intensity emitted by the anticathode is obtained as

$$T_A = \sum_{k=1}^{100} I_k + I_{K\alpha} + I_{K\beta} + I_L \quad (22)$$

The distribution of energy received by the detector. The intensity of radiation reaching the detector is reduced by absorption in materials inserted between the anticathode and the detector. For each absorbing atomic species the extinction coefficient is given by (17). For an absorbing species of thickness l_j the extinction for photons of energy qU is conveniently expressed as

$$\tau_j(U) l_j = n_j \frac{\Delta f_j(U)}{U} \quad (23)$$

where

$$n_j = \left[2r \frac{hc}{q} N \right] \frac{q}{hf_j} l_j \quad (24)$$

is a constant relating to the atomic species j the wavelength has been expressed as

$$\lambda = \frac{hc}{qU} \quad (25)$$

h being Planck's constant. The constant in brackets in (24) is evaluated as

Values for the excitation voltage of the characteristic spectra and the photon energy of emission lines are given by BEARDEN (1967)

Fig 3 a shows the calculated emission spectrum for a tungsten anticathode at 75 kV accelerating voltage Fig 3 b the calculated spectrum of 75 kV tungsten radiation filtered through 1 mm of copper and 1 mm of aluminium and Fig 3 c the calculated extinction spectrum of an iodine contrast medium For the case illustrated with a 5 mm thick contrast medium layer the contrast function k_v as calculated according to (32) to be $11.5 \text{ cm}^{-1} \text{ g}^{-1}$

SUMMARY

In order that high contrast be obtained in radiography the absorption of the radiation in differing parts of the object should be as different as possible The absorption in the object depends strongly on the wavelength A mathematical model is described which makes possible the calculation of the spectrum emitted by the roentgen tube and of the extinction in the object The method is applied to the contrast formation in videodensitometric angiography but can easily be extended to any kind of radiography

ZUSAMMENFASSUNG

Um den größten Kontrast bei der Röntgenaufnahme zu erhalten sollte die Absorption der Strahlung in den verschiedenen Teilen des Untersuchungsgegenstands so unterschiedlich als möglich sein Die Absorption im Objekt hängt wesentlich von der Wellenlänge ab Es wird ein mathematisches Modell beschrieben das es ermöglicht das von der Röntgenröhre emittierte Spektrum und die Extinktion im Objekt zu berechnen Die Methode wird bei der Kontrastbildung bei der videodensitometrischen Angiographie angewendet kann aber leicht auf jed Art von Röntgenaufnahmen ausgedehnt werden

RÉSUMÉ

Pour obtenir un haut contraste en radiographie l'absorption de la radiation dans les différentes parties de l'objet doit être aussi différente que possible L'absorption dans l'objet dépend beaucoup de la longueur d'onde Les auteurs décrivent un modèle mathématique qui permet de calculer le spectre émis par le tube de Roentgen et l'extinction dans l'objet Cette méthode est appliquée la formation du contraste en angiographie vidéodensitométrique mais peut facilement être étendue de toutes espèces de radiographies

REFERENCES

- BEARDEN J A X-ray wavelengths Rev. mod. Phys. 39 (1967) 78
 DUVILLIER A (1970) Quoted by REGLER (1977)
 HERTZEN P H editor Roentgen-röntgen and videodensitometry fundamentals and applications for blood flow and heart volume determination Georg Thieme Verlag Stuttgart 1971

- HÖGL H. Zur Dispersionstheorie der Röntgenstrahlen. *Z. Physik* 84 (1933) 1
- KULENKAAMPFF H. Über das kontinuierliche Röntgenspektrum. *Ann. Physik* 69 (1922) 548
- LANTZ B. A methodologic investigation of roentgen videodensitometric measurement of relative flow. To be published as a supplement to *Acta radiol.*
- and STRID K. G. Contrast formation in fluoroscopic videodensitometry. II. A comparison between theoretically computed and experimentally measured contrast. To be published in *Acta radiol. Diagnosis* 14 (1973)
- OSYKA P. and HEINTZEN P. New applications of television techniques for quantitative measurements in radiology and cardiology. Digest 7th Internat. Conf. Med. Biol. Eng. Stockholm 1967: 108
- REGLER F. Grundzüge der Röntgenphysik. Sonderbände zur Strahlentherapie. Band 21. Herausgegeben von H. Meyer. Urban & Schwarzenberg, Berlin/Wien 1937
- RUTSHAUSER W. Kreislaufanalyse mittels Röntgendensitometrie. Verlag Hans Huber, Bern 1969
- SIMON H., STUCKY J. P., SCHAD N., NOREDA G. and WELLMAYER J. Evaluation of roentgen videodensitometry for flow measurement in models and in the intact circulation. *Circulation* 36 (1967) 951
- SILVERMAN N. R. Television fluorodensitometry: technical considerations and some clinical applications. *Invest. Radiol.* 5 (1970) 35
- STRID K. G. Optimization of contrast in radiography. Gothenburg Inst. Phys. Rep. GIPR-061 (1972)
- STURM R. E., SANDERS J. J. and WOOD E. H. A roentgen videodensitometer for circulatory studies. *Fed. Proc.* 23 (1964) 303
- WEBSTER D. L. Large losses of energy by cathode rays: ratio of the probability of the two types. *Proc. Amer. Phys. Soc. Reno Meeting 1927. Physiol. Rev.* 30 (1927) 365
- WOOD E. H. and STURM R. E. Use of densitometry and electronic data processing for hemodynamic investigations by angiographic techniques. In: *Pathophysiology of congenital heart disease*. Edited by F. H. Adams, H. J. C. Swan and V. E. Hall. University of California Press, Los Angeles 1970
- — and SANDERS J. J. Data processing in cardiovascular physiology with particular reference to roentgen videodensitometry. *Proc. Mayo Clin.* 39 (1964) 649

CONTRAST FILLING OF THE LYMPHATIC SYSTEM OF THE LUNG THROUGH A PULMONARY VEIN IN THE DOG

C R PACHECO A CORTES and C RAMIREZ

A procedure for the demonstration of the lymphatic channels of the dog's lung was achieved by pressure injection of contrast medium into the right thoracic duct as reported in a previous paper (PACHECO et coll 1972). The results of continued efforts to evolve a suitable technique for the demonstration of the lymphatics of the lung and its eventual application in the human subject are now presented.

Material and Methods Ultrafluid lipiodol was introduced with a 5 mm ID polythene tube following left thoracotomy under general anaesthesia in 30 adult mongrel dogs divided into six groups each of 5 dogs. In the first group lipiodol was continuously injected into the pulmonary parenchyma. In the second group the segmental arteries and veins of the lingular segment were ligated before continuous injection of lipiodol into the pulmonary parenchyma. In the third



Fig 1



Fig 2



Fig 3



Fig 4

(For legends see opposite page.)

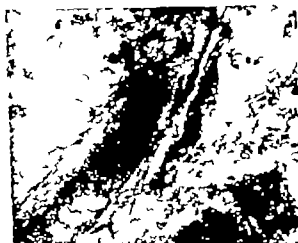


Fig. 3 Section of the left lower lobe (H & E $\times 40$) A lymphatic channel a slit like structure with contrast medium within its lumen (\rightarrow) lies adjacent to the wall of the bronchiole. Sections from the right lung presented similar appearances.

group the segmental bronchus of the lingula was divided and the proximal stump occluded the distal stump was injected. In the fourth group left subclavian artery—pulmonary artery anastomosis (Blalock Taussig) was performed and the lingular vein ligated while the artery was continuously injected. In the fifth group the vein of the dorsal segment of the lower lobe was tied and the artery continuously injected. Finally in the sixth group ligation of the artery and occlusion of the vein of the dorsal segment of the lower lobe were followed by continuous injection of lipiodol into the vein on the pulmonary side.

Pulmonary roentgenography was carried out during and after the procedure described and sections of both lungs were taken from all dogs.

Results

No lymphatic channels were evident in the chest films of the dogs from the first five groups. Lymphatic channels were present in the initial chest films of the dogs in group 6 (Fig. 1) and then serial films were started. After approximately 2.5 ml of contrast medium being injected into the segmental vein the

For 1 The artery and vein of the dorsal segment of the left lower lobe were ligated and 10 ml ultrathin lipiodol injected into the vein on the pulmonary side. The lymphatic channels of the lobe are beginning to fill.

Fig. 2 The lymphatic network becomes more obvious as more lipiodol is injected through the vein.

Fig. 3 After injection of 15 ml lipiodol through the vein of the dorsal segment the lymphatic channels of the left lower and upper lobes are evident.

Fig. 4 Further injection (10 ml). The lymphatic channels of the contralateral lung are filled and the pulmonary veins are defined.

contrast medium appeared in the lymphatic channels as a very delicate network emerging from the vein and running into the periphery as more lipiodol approximately 10 ml, was injected into the vein, the whole lymphatic network of the ipsilateral (Figs 2, 3) and then also of the contralateral lung was filled. Finally, after 18 to 20 ml of contrast medium being injected, the pulmonary veins of the contralateral lung were demonstrated (Fig 4). The sections of lung disclosed contrast medium inside the lymphatic channels (Fig 5).

Discussion

The lymphatic channels of the lung in the dog have been filled by pressure injection of ultrafluid lipiodol into the vein of the dorsal segment of the left lower lobe after ligation of the vessels of the segment. That the contrast medium lay within the lumen of the lymphatics and not in the veins, was indicated by the appearances in the films and by the sections of lung. The roentgenographic appearances are characteristic, the lymphatics being represented as a delicate network formed by rigid lines, while the veins are tortuous. The outlining of the lymphatic channels of the contralateral lung may be explained as due to anastomoses between the two lungs probably made patent by the abnormal conditions imposed by the thoracotomy, the assisted respiration and the injection of lipiodol under pressure.

This procedure represents another step in continued efforts to develop a technique for demonstrating the lymphatic channels of the human lung both in health and disease.

SUMMARY

A procedure for demonstrating the lymphatic channels of the lung in the dog by the injection of lipiodol under pressure into the vein of the dorsal segment of the left lower lobe after ligation of its artery is described. The lymphatic network of the ipsilateral and the contralateral lung are filled in turn. The method represents another step in continued efforts to develop a suitable means of outlining the lymphatics in the human lung.

ZUSAMMENFASSUNG

Es wird ein Verfahren zum Nachweis der Lymphbahnen der Lunge am Hund durch Injektion von Lipiodol unter Druck in die Vene des dorsalen Segments des linken Unterlappens nach Ligatur dessen Arterie beschrieben. Das lymphatische Netzwerk der seitengleichen und gegenseitigen Lunge füllen sich nacheinander. Die Methode bildet einen weiteren Schritt bei den ununterbrochenen Anstrengungen geeignete Verfahren zur Darstellung der Lymphwege der menschlichen Lunge zu entwickeln.

RÉSUMÉ

Les auteurs décrivent une technique de mise en évidence des canaux lymphatiques du poumon sur le chien par injection de lipiodol sous pression dans la veine du segment dorsal du lobe inférieur gauche après ligature de son artère. Les réseaux lymphatiques pulmonaires du même côté et du côté opposé sont opacifiés successivement. Cette méthode représente une autre étape dans les efforts continus pour mettre au point un moyen convenable de mettre en évidence les lymphatiques du poumon humain.

REFERENCES

- PATTECO C. R., CORTES A. and RAMIREZ C. Contrast filling of the pulmonary lymphatic system in the dog. *Acta radiol. Diagnosis* 12 (1972) 81.

TRANSVERSE AXIAL TOMOGRAPHY IN THE DETERMINATION OF LUNG VOLUME IN KYPHOSCOLIOSIS

LARS BJÖRK

Kyphoscoliosis frequently causes considerable deformity of the chest and restriction of its ventilatory capacity. Whether the restriction in capacity be caused by diminution in the volume of the lungs or by functional disturbances due to the deformity of the chest or a combination of both is not obvious. BERGQVIST *et coll.* (1959) and HOLMES (1967) stated that one of the lungs becomes compressed and the other expanded. Standard roentgenograms are not entirely satisfactory in measuring the volume of the lungs in these patients (Fig. 1). The deformity is such that even a rough estimate of the volume of each half of the thoracic cavity is unreliable and renders the results of radiospirometry and lung scans difficult to interpret. The previous employment of transverse tomography for investigating the topographic anatomy in kyphoscoliosis (LÖNN, 1962; BJÖRK *et coll.* 1967) has been extended to determine the volume of each lung in a small material of the same condition and the results are now reported.

Method and Material. The patients sat with the arms raised above their heads on the rotating chair in the tomograph. (For detailed description of the

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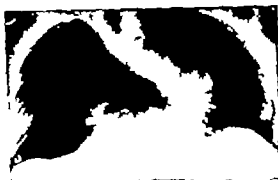


Fig. 1 P.A. chest roentgenogram of 43 year old woman (Case 2) with marked chest deformity due to scoliosis. Assessment of volume of right and left lungs is not possible.



Fig. 2 Transverse axial tomogram in hilar region of the same patient as in Fig. 1. The cross-sectional areas of right (17 cm) and left (180 cm) lungs are nearly the same.

technique see GEDAUER & SCHÄNEN 1955.) Axial transverse tomograms of the entire thoracic region were obtained in each patient at 2 cm intervals. The patients were instructed to take a deep breath and hold it for each roentgen exposure. The horizontal cross sections of the right and left lungs were traced in each tomogram (Fig. 2). The area of each section of the lung was measured by planimetry: three measurements were made and the mean value used for further calculations. The differences between the three measurements were usually small and never exceeded 2 per cent. The volume of each lung was calculated by the Simpson principle by adding the areas measured in the tomograms (corrected for magnification) for the right and the left lungs and then multiplying this by two: the distance between the tomographic layers. The volume of each lung was thus obtained and expressed in millilitres.

Table

Comparison between tomographically and spirometrically determined lung volumes in 6 patients with kyphoscoliosis

Case	Type of scoliosis	Transverse tomography volume (ml)				Spirometrically determined total lung capacity (ml)	Calculated normal total lung capacity (ml)
		Right lung	Left lung	Quotient right/left lung	Total lung volume		
1	right	1040	1760	0.52	2300	2800	5700
2	left	1060	1210	0.88	2270	3000	3000
3	right	980	970	1.07	1900	2500	3700
4	right	2150	1950	1.10	4080	3900	7200
5	left	2200	2340	0.94	4540	4300	6800
6	left	940	910	1.03	1850	2100	6100

The method has been applied in 6 patients with severe deformity of the chest due to kyphoscoliosis.

Results

A marked reduction in the total lung volume from the normal value expected from the size and age of the patient was evident (Table). On the other hand no marked difference in size between the right and left lung was apparent which means that the reduction in volume was fairly symmetric. The quotient right/left lung also appeared to vary independently of whether right or left scoliosis was present.

Fairly good correlation also existed between the total lung volume measured by tomography and total lung capacity determined by spirometry (Table Fig 3).

Discussion

The accuracy of this method of calculating lung volume was tested by placing a plastic container roughly shaped to simulate a lung in the thorax of a human skeleton. Further plastic material was added on the outside to simulate soft tissues and put in the thorax to represent the heart and mediastinum. This model was tomographed in the same way as the patients and the volume calculated from the tomograms. The volume of the plastic container was then determined by filling it with water: its true volume was always larger than that

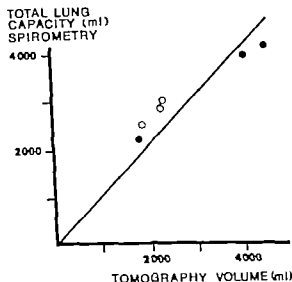


Fig 3 Correlation between total lung capacity measured by spirometry and total lung volume indicated by transverse tomography ○ women ● men

obtained by calculation from the films by the Simpson method the error being between 5.5 and 6 per cent. This indicates that the volume of the lungs or rather the pleural cavity can be measured with reasonable accuracy by the transverse tomographic method. It is on the other hand obvious that a larger error should occur in patients in whom the margins of the lungs are sometimes more difficult to trace than those in a plastic container. Three determinations in each tomogram of the cross section area of the lung in that tomographic layer were therefore performed to test the observation error and as mentioned above the errors between different determinations were always small. It appears that this method may be employed for the assessment of volumes of organs of complicated shape. A prerequisite is of course that the absorption difference between the volume to be measured and surrounding tissue be enough to be clearly demarcated in the tomograms with the lungs and the chest no enhancement of contrast is necessary but with the method applied to other organs such techniques may be useful.

The findings in this small material that both lungs had approximately the same volume in patients with severe chest deformity due to scoliosis is contrary to previous statements (BRADORSKY et coll. HOLMES) that one of the lungs should be more compressed than the other. This illustrates the difficulty in assessing the volume of the lungs in conventional roentgenograms. An ordinary p.a. film of a patient with severe scoliosis gives the impression that one lung is more reduced in volume (Fig. 1) whereas transverse axial tomography demonstrates that both lungs have nearly the same volume (Fig. 2 Table). When differences occur they also seem to be independent of the type of scoliosis.

Axial transverse tomography should therefore be of value in the preoperative evaluation of patients with deformity of the chest caused by scoliosis. The method affords information both on the topographic anatomy (Louny 1962 and others) and the volume of the two lungs. It must of course be realized that the functional capacity of one lung may be less than that of the other lung due to factors such as differences in mobility of the chest wall and diaphragm. However methods available for determining the functional capacity of each lung are difficult to apply in these patients. The distorted geometry makes radiosprometry unreliable and the abnormal anatomy makes bronchosprometry difficult.

SUMMARY

Axial transverse tomography enabled the lung volume in 6 patients with marked chest deformity due to scoliosis to be measured. The total volume correlated well with the total lung capacity determined by spirometry. The volumes of the right and left lung proved to be almost similar with small differences unrelated to the type of scoliosis.

ZUSAMMENFASSUNG

Die axiale Transversaltomographie ermöglichte es das Lungenvolumen von 6 Patienten mit markierter Brustdeformation infolge einer Skoliose zu messen. Das Gesamtvolumen stimmte gut mit der spirometrisch gemessenen Gesamtlungencapazität überein. Die Volumina der rechten und linken Lunge waren nahezu gleich mit geringen Unterschieden, die nicht mit dem Typus der Skoliose in Zusammenhang standen.

RÉSUMÉ

La tomographie axiale transverse a permis de mesurer le volume pulmonaire chez 6 malades atteints de déformation thoracique importante due à une scoliose. Le volume total était en bonne corrélation avec la capacité pulmonaire totale déterminée par spirométrie. Les volumes des poumons droit et gauche se sont révélés être presque semblables et de petites différences sans relation avec le type de scoliose.

REFERENCES

- BERDOFFSKY E. H., FURNO G. M. and FREEMAN A. P. Cardiorespiratory failure in kyphoscoliosis. *Medicine* 38 (1959) 263.
- BJÖRK V. O., BJÖRK L. and HILTE R. Ost plasty thoracoplasty as palliative treatment of thoracic deformity in scoliosis. *Scand. J. thorac. cardiovasc. Surg.* 1 (1967) 181.
- GERAUER A. and SCHÄFER A. Das transversale Schachtelerfahren. Georg Thieme Verlag Stuttgart 1955.
- HOLMES JR. F. W. Thoractomy in the patient with dorsal scoliosis. *Dis. Chest* 32 (1967) 397.
- LOUNY H. Transversal tomography in the examination of thoracic deformities (funnel chest and kyphoscoliosis). *Acta radiol.* 37 (1962) 49.

MOULDING OF THE PELVIS DURING LABOUR

HANS OHLSEN

Up to the middle of the nineteenth century opinion fluctuated between the theory accredited to Hippocrates that simple widening of the symphysis occurs at the first pregnancy and delivery and the view that the pelvic joints are rigid. Several authors (e.g. LYACH) have suggested that true widening of the symphysis and sacroiliac joints occurs only in pathologic cases. Around about 1870 it was generally accepted that opening of the pelvic joints might permit relaxation of the pelvis. As early as 1812 LE GALLON observed marked widening of the pelvis towards the end of pregnancy and during actual parturition in the guinea pig which he took to be normal. ZAGLAS (1851) drew attention to the possibility of other movements in the pelvic joints when he demonstrated that rotation of the ilium about a transverse axis through the sacroiliac joints occurs in women. On flexion of the hip joints the sagittal diameter of the pelvic outlet may thereby increase and the true conjugate diminish though to a lesser degree. These results have been variously confirmed by a number of authors e.g. DUNCAN (1854) WALCHER (1889) and VON KUTNER (1898).

The advent of roentgenography made it possible to obtain more exact information on the dimensions of the pelvis and their changes during pregnancy and labour.

LYNCH (1920) claimed to have found that widening of the sacroiliac joints although not of the symphysis pubis were almost constant features of pregnancy. He published two films obtained during labour with the head during and after internal rotation. One film depicted the head fully rotated towards the pelvic floor while in the other it lay at about the level of the ischial spines, in both instances the sacroiliac joints were obviously wider than usual. HEYMAN & LUNDQVIST (1932) in an investigation on the width of the symphysis pubis during pregnancy and parturition described 6 cases in which films had been obtained on more than one occasion during the early stages of labour none revealed any significant increase in the width of the symphysis pubis.

ABRAMSON *et coll* (1934) in a selected group of cases with signs ascribed to pelvic instability reported that the width of the symphysis was little affected by parturition. ROBERTS (1934) stated the same thing but added that there seemed to be no widening of the symphysis pubis during the first stage of labour although his series was small and inconclusive. THORP & FRAY (1938) in the first attempt at a systematic radiographic examination during labour refuted the earlier view that no widening of the pelvis occurs. They observed an increase in the width of the symphysis pubis in 34 out of 78 cases (44 per cent) at the first stage of labour when compared with measurements in the last trimester. The mean increase was 5 mm and the maximum 12 mm. No change in the area of the pelvic inlet could be demonstrated in spite of the presence of separation.

Slight widening of the symphysis pubis during pregnancy has been demonstrated by HEYMAN & LUNDQVIST (1932), ABRAMSON *et coll* (1934) and ROBERTS (1934). YOUNG (1940) in 'Relaxation of the pelvic joints in pregnancy' a much quoted review summarised the knowledge up to that time as roughly 1) pregnancy leads to a relaxation and widening of the symphysis pubis, 2) a great variation in the degree of this widening exists, 3) the widening commences during the first half of pregnancy and in general does not progress after the last 2 months, it is not increased by labour, 4) the width of the symphysis pubis diminishes after labour and approaches the pre-pregnant measurement and 5) there is some evidence of a similar change in the sacroiliac joints.

BORELL & FERNSTROM (1957 a) examined the course of events during labour with the aid of a p and lateral roentgenograms in 40 cases. They found that the symphysis pubis was displaced downwards as the foetal head passed through the pelvic inlet and upwards as it passed through the outlet. The displacement could be as much as 25 mm. The true conjugate was invariably larger (by as much as 10 mm) when the head passed through the inlet than when it was in the outlet. The sagittal diameter of the outlet was likewise more when the head passed through the outlet. In most subjects the difference in the sagittal diameter of the outlet was more than 10 mm and in one it increased by 20

Table 1

The 29 cases in which changes in the pelvic dimensions during labour were investigated VOA = vertex presentation occiput anterior position VOP = vertex presentation occiput posterior presentation

N	of cases	Presentation and position	Course of labour	Age
20	p	primiparae		24 (18-34)
18		VOA	Normal	
1		VOA	Normal + scutum extraction	
1		VOP	Normal	
9	m	multiparae		29 (20-39)
7		VOA	Normal	
1		VOA	Complicated (inlet contraction)	
1		VOA	Complicated infant died (outlet contraction)	

mm. The changes were produced by rotation of the hip bone in relation to the sacrum. A gliding movement of the sacrospinous joints probably occurs during labour as it does during pregnancy (BOWELL & FERNSTROM 1957 a). Forward displacement of the symphysis pubis was directly demonstrated as the head passed through the inlet in a case in which the true conjugate was reduced. They observed no change in the transverse diameter of the inlet (1957 b). Widening of the symphysis and sacrospinous joints by a few millimeters was evident in some subjects but this was not regarded as significant. The fact that little if any change in the sagittal dimensions during and after parturition was sometimes recorded suggested the possibility of a rigid pelvis.

RUSSELL (1969) in an investigation of 96 cases in the last trimester found by HARTLEY's technique (1958) an increase of 7.5 mm (± 3.5 mm) in the bispinous measurement in the Chamard-Lapine compared with the supine position. No such increase was evident about 6 weeks after delivery. These results together with the view presented in modern textbooks (BAROETT 1970 GREENHILL 1963 HELLMAN & PRITCHARD 1971) that no widening of the pelvis occurs during the actual labour prompted the present investigation.

Material. This consisted of the films of 29 cases: 20 primiparae and 9 multiparae, examined in 1955-1957 by BOWELL & FERNSTROM. The mean ages of the two groups were 24 and 29 years (Table 1). The material was not selected — apart from the exclusion of films the quality of which did not permit of

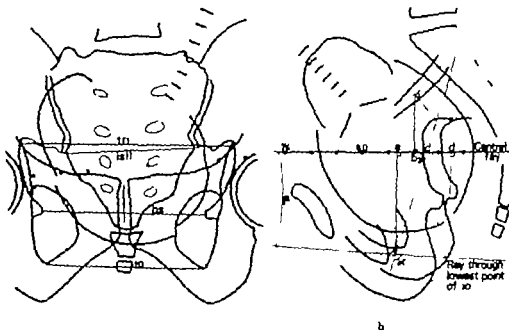


Fig. 1 a) A p view of the pelvis. Transverse diameters: tr transverse inlet ml intermacroscopic bispinous io interobturator b) Lateral view (lead markers indicate the scale for the focus-film distance) $\beta = \tan^{-1} \frac{a}{b}$ $\gamma = \tan^{-1} \frac{c}{d}$ (—a) $\alpha = 100$ — β —

a reliable identification of the reference points (bispinous distance and inter-obturator distance) and the inclusion of films in which the greatest width of the foetal head could be recorded above and below the level of the sacral spaces. Inferior film quality in 4 cases prevented registration of the bispinous distance and in another the interobturator measurement was not recorded but they were included in the series when the other reference points could be identified. The true conjugate in one case measured 8.5 cm and labour was difficult, a small necrotic area developing in one parietal bone. The outlet was small in another case in which the infant died with confirmed severe deformation of the head (Borell & Fernstrom 1958 b cases 1 and 3). All the 29 cases were of vertex presentations, in one of them there was an occiput posterior position at delivery and in the others an occiput anterior position. All cases with the sole exception of the one with the outlet contraction gave birth to apparently healthy infants.

Method. The roentgenographic technique used by Borell & Fernstrom consisted in taking a p and lateral films at intervals of 0.5 seconds by means of an Elekma bi plane roll film changer. Such pairs of films were exposed

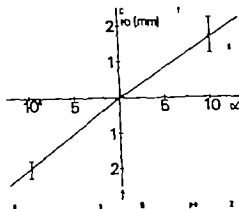


Fig 2 Graph for correcting distance c when the angle α (see Fig 1 b) is changed in relation to its value in the first pair of films

between labour pains and during successive phases as the head passed through the birth canal. The focus film distance was kept constant at 100 cm. The dose to the maternal gonads was about 2 to 3 R and to the foetal gonads less than 0.1 R (BOWELL *et al.* 1958 c). It should be mentioned that the series was collected in the mid fifties at which time it was not considered that such doses incurred any risk.

Measurement procedure. As the patient changed position during the course of the examination the reference points were displaced in relation to the central rays of the overcouch and lateral tubes and the primary magnification may therefore have varied from one film pair to another. However because two perpendicular planes were used the magnification for each film could be calculated and thus enabled a high level of accuracy for measurements to be achieved. All the reference points were marked on the films with a pencil. The distance on the film was recorded to the nearest tenth of a millimetre; thus, in absolute figures implies a false accuracy of measurement. The greatest measurement error was incurred in marking the reference points in the a.p. films. A control of the accuracy in which 16 bispinous distances in 6 different subjects were measured by four investigators to the nearest tenth of a millimetre indicated that the different ranges in the 16 groups were on average 1.6 mm and if one diverging group of measurements were excluded became 1.4 mm. With a reduction for magnification of about 0.85 the figure 1.4 was further reduced to 1.2 mm. The maximum measurement error for this distance therefore without no doubt did not exceed 2 mm. At least the same accuracy of measurement can be expected for the interobturator distance (see below). Another control of the accuracy in which 15 distances marked in advance by the author were

measured by eight investigators to the nearest tenth of a millimetre revealed that the range did not exceed ± 0.1 mm in the 15 groups. This measurement error is thus negligibly small compared with that incurred in marking the reference points. Angles used for the correction were calculated geometrically to the nearest degree. The values in the final evaluation were given to the nearest whole number.

Bispinous diameter The bispinous diameter was taken as between the extreme medial points of the respective ischial spines in a p films and corrected for magnification against simultaneous exposed lateral films (Fig. 1)

Bituberous distance (posterior) Model experiments with 7 female pelvis revealed that none of the methods known to the author that might have been considered applicable to this film material could in fact be used. No fixed reference point exists on the ischial tuberosities and the distance between for instance, the lowest tangential points in the a p film changes considerably for only a small alteration in the inclination of the pelvis or its displacement in a craniocaudal direction. A distance that, on the other hand, changes relatively little, and then almost linearly when the projection is changed was that between the lowest point of the obturator foramen on each side (so Fig. 1 a).

The pelvic skeleton in one of the experiments was placed on a plate inclined at about the same angle as the patient lying supine with the legs lightly flexed. The central ray was directed on the midline, perpendicular to the film and the line joining the lowest point on each obturator foramen (so, position 0). The tube focus was moved parallel to the film plane exactly 10 cm cranially (position 1) and caudally (position 2). One film was exposed in each of these 3 positions. The pelvis were never disturbed. The focus-film distance was kept constant at 100 cm; the object (so) film distance was measured directly in position 0; the magnification factor for positions 1 and 2 was taken as the same as that for position 0; the difference being negligible. The change in the angle from position 1 to 2 for the path of the ray tangential to the lowest point of the foramina was obtained geometrically and a graph drawn (Fig. 2). From this curve so was corrected with respect to the change in angle α (Fig. 1 b) for the ray in the various films obtained at intervals during labour. In each pair of films (a p and lateral) so was measured, and correction made for the magnification. The angle α was calculated and by means of the graph so corrected with respect to the change in α from its value in the initial (reference) pair of films. Account was thus taken of the magnification, the change in inclination of the pelvis and any displacement of the patient in relation to the central ray.

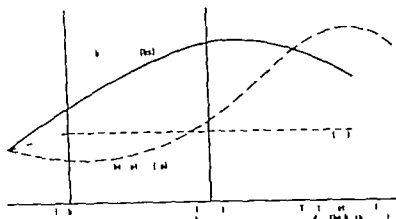


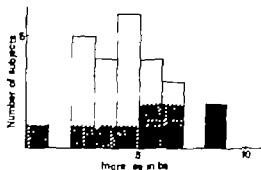
Fig. 3 Graph of movement for changes in various transverse pelvic diameters during labour

Sacroiliac joints Since BORELL & FERNSTROM (1957 a) indicated that a gliding movement may also occur in these joints during labour it was obvious that their actual width could not be measured directly. The intersacroiliac distance was therefore used instead (Fig. 1 a) and a correction for the magnification then made against the corresponding lateral film. This dimension incurs a risk of a measurement error because of difficulty in establishing exactly the position of the lower border of the sacroiliac joints in lateral films: this error was estimated at not more than ± 1 cm. An observed distance of 11 cm for the intersacroiliac distance and a focus-object distance of about 89 cm would give 9.68 cm and 9.90 cm respectively after correction for magnification: that is to say for an estimated error of ± 1 cm after correction a resultant error of about ± 0.1 cm is obtained. The presence of any gas in the joints was recorded.

Symphysis pubis The width of the symphysis pubis was measured in the various cases: in the individual case the reference points were the same in the various a.p. films. As above a correction was made against the lateral film of the pair. The presence of any gas in the joint was recorded.

Transverse inlet The diameter of the transverse inlet was measured in a p. films and corrected for the magnification (Fig. 1). The measurement of this diameter is liable to contain an error because the pelvic inlet is not delimited by a well defined osseous border and the reference points may therefore change if the patient be lying slightly obliquely. Where possible therefore the transverse distance between the lateral upper margin of the acetabulum was measured. It, too, was corrected for magnification against the lateral film.

Fig 4 Increase in the bipinous measurement during labour in 25 subjects (mean 4.4 mm) in relation to the absolute initial bipinous diameter in the respective subjects. Bipinous diameter ≤ 9.5 cm (heavy line bars) and bipinous diameter > 10.0 cm (light line bars)



Results

The changes were represented graphically to obtain an impression of any variation in the transverse dimensions (transverse inlet, *bs* and *io*) when the foetal head passed through the birth canal (Fig 3). The graphs for the various dimensions are mean curves calculated from smoothed individual curves.

Bipinous distance (*bs*) A small increase during labour amounting on an average to 4.4 mm (range 0.9 to 8.1 mm) was evident in all but one of the 25 subjects in whom the bipinous diameter could be recorded (Fig 4).

A definite tendency occurred in most of the cases in this small series in which only different phases of labour were observed for the bipinous diameter to increase gradually until the maximum presenting circumference of the head had passed the level of the ischial spines after which bipinous diameter usually diminished (Fig 6). No obvious difference between the primiparae and multiparae was apparent.

The change in the bipinous dimension was larger in the subjects with a bipinous diameter 10.0 cm or less than in the subjects with a diameter exceeding 10 cm. The difference in the change was significant ($p \sim 0.025$) (Fig 5). Another factor that would presumably have a bearing on the measurement would be the size of the foetal head, especially the biparietal diameter in a vertex presentation. There was no correlation between the increase in the bipinous distance and the size or moulding of the foetal head, but it must be emphasized that the material in this respect is too small for any conclusions to be drawn. Values for the various measurements appear in Table 2 for the 4 cases with a small bipinous distance mentioned in connection with figures 4 and 5.

Interobturator distance (*io*) The interobturator distance was chosen because of measurement factors and to estimate the transverse diameter of the pelvic

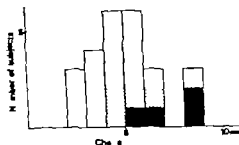


Fig. 5 Changes in the bispinous measurements during labour in 25 subjects (mean 0 mm). Changes = $bs_{max} - bs_1$ or bs_{min} . Bispinous diameter ≤ 9.3 cm (heavy line bars) and bispinous diameter 9.4 to 10.0 cm (dotted bars)

outlet as far down as possible consistent with precision. In all primiparae the distance increased during labour by a mean of 5.2 mm (range 1.5 to 9.3 mm). Two thirds of the cases displayed an initial reduction in the interobturator distance when the foetal head was above the plane through the ischial tuberosities (Fig. 7) in 13 out of 28 cases this reduction exceeded 1 mm with a maximum of 3 mm.

In only one of the 24 cases in which both the bs and io could be measured was io_{min} recordable at an earlier phase of labour than bs_{min} in this one (Case 26) with a rather small bispinous diameter the interobturator distance at first decreased considerably and then remained constant. The bs_{min} and io_{min} in 6 cases were recorded at the same phase of labour but in 4 of these the bispinous distance increased before the interobturator distance and for the other 2 the curves were parallel. The io_{min} in all but 2 of the 24 subjects occurred when the lowest part of the head was at least 4 cm below the ischial tuberosities in contrast to the bs_{min} which in 14 cases occurred before this part of the head passed through the limit 2 cm below the tuberosities.

Table 2

Separate report for 4 subjects just at to have small bispinous diameter (< 9.3 cm)

	Case No			
	2	14	19	29
B parietal diameter of the foetal head (cm)	9.3	9.1	8.9	9.6
Bispinous diameter bs (cm)	9.2	9.3	9.3	8.3
Increase in bs (cm)	0.6	0.5	0.8	0.8
Total moulding of the foetal head (cm)	0.8	0.9	1.1	2.0

Pathologic

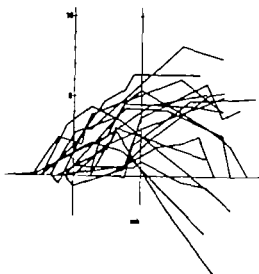


Fig 6 Variation in the bispinous measurements during labour in 17 primiparae

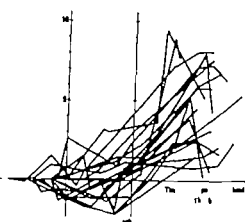


Fig 7 Variation in the interobturator measurement during labour in 19 primiparae

Sacroiliac joints Gas was present in the lower part of the sacroiliac joints in 2 cases so long as the lowest part of the head was located above the ischial spines, in 3 cases when the head was between the spines and the tuberosities, and in as many as 18 out of 29 cases (62 per cent) when the lowest part of the head was below the ischial tuberosities (Fig 8). In 25 out of 26 cases in which the intersacroiliac distance could be measured an increase during labour averaged 4.2 mm (range 0 to 9.1 mm) (Fig 9). In the exceptional case in which the interobturator distance decreased initially and then remained constant (Case 26) the intersacroiliac distance also decreased about 4 mm. The maximum for the intersacroiliac distance often about coincided with the maximum interobturator distance. Moreover a definite statistical association ($p < 0.01$) between the increase in these distances was evident.

Symphysis pubis A streak of gas was observed in the symphysis pubis during the beginning of labour in 9 out of 23 cases (39 per cent). When the lowest part of the head was between the ischial spines and the tuberosities gas was definitely present in somewhat less than one fifth of the subjects and, in 6 out of 9 with gas initially it decreased or disappeared during this phase of labour. When the head was below the ischial tuberosities the symphysis could be examined for the presence of gas in only 12 cases; in the others the face or cervical spine was superimposed. In 2 of these cases gas was however present earlier in labour (Fig 8).

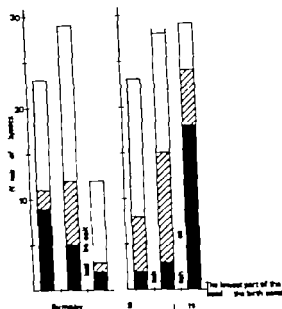


Fig. 8. Gas in the symphysis pubis and sacroiliac joints during different phases of labour in 79 subjects. ■ marked ■ slight □ probably some □ none not assessed

An increase of a millimetre or so in the width of the symphysis pubis was occasionally evident during labour after correction for magnification although in no case did the true increase amount to 3 mm. In 4 cases the corrected width of the symphysis was at least 7 mm — in one of them 10 mm — and was thus abnormal to judge from the values given by several other authors (ABRAMSON *et coll.* 1934 HEYMAN & LUNDQVIST 1932 ROBERTS 1934 WILLIAMS 1955). None of these 4 cases exhibited any change in the width of the symphysis pubis during the course of labour.

Transverse inlet (tri) For reasons given above an error occurred in the measurement of this dimension. Extremely small changes if any were usually recorded. In only one out of 21 cases was the variation greater than 3 mm when it was 4 mm. In 6 out of the 9 cases in which both the diameter of the transverse inlet and the transverse distance between the upper borders of the acetabula were measured curves for these two dimensions followed each other. The error of measurement was presumably relatively small in these 6 cases since the reference points were located close together and should for the most part have followed each other and the variation in the diameter of the transverse inlet was less than 2 mm.

Symphysis pubis No definite widening of the symphysis was evident as the head passed through the distal part of the pelvis, nor was this present in those cases in which the greatest circumference of the head was at first located above or within the pelvic inlet, and in which the passage of the head through the inlet could thus be followed. This appears to be consistent with the findings of HEYMAN & LUNDQVIST in the 6 cases mentioned above. No comparison can be made with the widening of the symphysis pubis observed by THORP & FRAY since these authors determined the width before and at the beginning of the first stage of labour. The present results suggest rather that minor compression of the symphysis pubis may sometimes occur as the head passes through the distal part of the pelvis. Any gas present in the joints — first reported in pregnancy by MAONUSSON (1937) — decreased during labour so that while it was fairly common at the beginning (in about 40 per cent of cases) it was recorded in only 17 per cent when the lowest part of the head was located between the ischial spines and the tuberosities. The former initial frequency would appear to be comparable with WILLIAMS' (1955) value of 11.5 per cent for gas during the last trimester and the 30 per cent reported by CAMMEL & AARON (1956).

Sacroiliac joints (mil) The actual sacroiliac joints often widened little, if at all. For the reasons given above, however, the width of the articular space was never closely examined. On the other hand, an increase in the intersacroiliac measurement nearly always averaged 4 mm.

It should be noted that the plane of the articular surface in the lower part of the joint is usually directed obliquely backwards and medially, and the two planes — one for each joint — then intersect at an acute angle. At the end of labour almost all patients had moved cranially relative to the central beam and the tangential point at the lowermost part of the ilium next to the joint would then move a millimetre or so medially. No correction for this was made; the recorded mean increase of 4 mm in the mil distance should thus probably be a millimetre or so greater.

The obvious discrepancy between the increase observed in the mil and the absence of a corresponding widening of the actual articular space suggested the following explanation. During the widening in the posterior circumference of the ring there must be a backward displacement of the sacrum which is wedge shaped with the vertex directed dorsally. The widening then cannot be seen as a widening of the articular spaces. If the joint be regarded as a closed volume when the sacrum is displaced dorsally an increase in this volume would be needed to maintain the width of the space: the reduced pressure would thus lead to the presence of gas. Gas was observed in the distal part of the sacroiliac

joints as the head passed through the pelvic outlet it was much less common when the head was in the upper part of the birth canal than in the lower part when it was evident in 60 per cent of the cases. The low initial frequency of gas is consistent with RUSSELL's (1955) figure of 2 out of 200 consecutive patients examined during pregnancy.

Transverse inlet (tn) The difficulty in measuring this dimension prevented definitive conclusions being drawn but unlike the other dimensions, this probably underwent only a negligible change.

Overall analysis of pelvic mouldability during labour BORELL & FERNSTROM were the first to demonstrate convincingly that the sagittal dimensions change to facilitate the passage of the foetal head in the birth canal during labour irrespective of the patient's position.

This change was made possible by rotary movements about a transverse axis probably within or in the vicinity of the sacroiliac joints — sometimes connected with gliding of the sacrum in relation to the hip bones. The present examination of the original series of films disclosed a simultaneous small increase in the transverse dimensions in the distal pelvis, usually amounting to about 0.5 cm. This increase was previously refuted but it has recently been considered a possibility with postural changes during the last trimester (RUSSELL 1969).

The examination has also indicated that the movement that almost invariably occurs in the sacroiliac joints — which is consistent with the findings of GOLDTHWAIT & OSGOOD (1905/1907) on anatomic grounds — provides an extremely complex pattern of motion. There must be movements about more or less transversely oriented axes in the vicinity of the upper part of the sacroiliac joints.

The results point fairly conclusively to a gradual adaptation (increase) of both sagittal and transverse dimensions — the latter of a minor degree — as the foetal head passes through the birth canal. The biparietal diameter thus increased slightly before the increase in the interobturator distance (so). Simultaneously with a rise in the latter an increase in the intersacroiliac distance and the presence of gas in the joints occurred. In addition indirect evidence of backward gliding of the sacrum was recorded; this has also been reported by WARE and BORELL & FERNSTROM.

The movement in the pelvic joints and its effect on the pelvis (birth canal) as a whole has long concerned authors such as ZAGLA, LABOUR, GOLDTHWAIT & OSGOOD, WARE, BORELL & FERNSTROM and RUSSELL. No analysis of the total pattern of movement in the pelvic joints during passage of the foetal head through the birth canal has previously been made.

The complex movement observed is inconsistent with the movement theory

of LABORIE (1862) thus there is no evidence of a hinge movement about a sagittal axis through the symphysis but rather one about a variable axis, one for each hip bone similar to the variable transverse axis of rotation reported by WEISL (1955) for movements in the sacroiliac joints. The variable axis must however lie in an oblique dorso-medial plane. For these reasons and because of gliding the sacroiliac joints cannot be regarded as ball joints. With this pattern of rotation the prerequisites as were suggested by RUSSELL (1969) on the basis of the LABORIE theory are present for an increase in the pelvic outlet without obvious diastasis of the pelvic joints. From the results published by BORELL & FERNSTROM and his own findings RUSSELL stated that possibly a 20 to 30 per cent increase in the available area in the pelvic outlet occurs.

The present results and those of BORELL & FERNSTROM in the same series suggest that moulding of the pelvis usually occurs during labour, the gradual adaptation leading to an increase of about 20 per cent in the area available in the outlet: this is provided that, e.g. the sagittal diameter of outlet increases by between 1 and 2 cm and the transverse diameter by 0.5 cm.

The cause of the moulding demonstrated probably lies in an interaction of various factors whose detailed analysis has so far not been attempted. It has previously been considered that direct pressure of the foetal head cannot cause moulding of the pelvis, a view based on, for instance, the results obtained by POUILLET (1864). This author stated that great force was required to rupture the symphysis pubis in women who had died during puerperium (see LYNN). LABORIE (1862) presented a theory of a hinge movement implying that when the foetal head reaches the pelvic outlet the bituberous diameter increased through direct pressure, simultaneously with a decrease in the distance between the iliac crests.

Although the axis of the movement in the LABORIE theory had not been confirmed in this investigation, evidence exists that direct pressure of the foetal head contributes to the moulding. The bispinous measurement thus proved to increase significantly more in cases with a small bispinous diameter than in those in which it was large.

SUMMARY

The complex moulding of the bony pelvis produced by its gradual adaptation to the passage of the foetal head during labour has been investigated in the same basic series used by BORELL & FERNSTROM (1957-1958) to demonstrate changes in the sagittal diameters. The transverse diameters in the distal part of the pelvic canal increased by about 0.5 cm in most of the 29 cases and together with the increase in the sagittal diameter of outlet produced an enlargement of about 20 per cent in the total area available.

ZUSAMMENFASSUNG

Die komplexe Formung des knöchernen Beckens hervorgerufen durch die graduell Anpassung an den Durchtritt des kindlichen Kopfes während der Geburt wurde bei der gleichen ursprünglichen Serie der von BORRILL & FERARSTROM (1957-1958) zum Nachweis der Veränderungen im sagittalen Diameter angewendet worden waren untersucht. Die transversalen Diameter des distalen Teils des Beckenkanals stiegen bei den meisten der 29 Patienten um erw. 0.5 cm dadurch zusammen mit dem Anstieg des sagittalen Durchmessers der gesamtzugänglich Platz um erw. 20 Prozent anstieg.

RÉSUMÉ

Le modelage complexe du bassin osseux produit par son adaptation graduelle au passage de la tète fœtale au cours du travail a été étudié sur les mêmes séries de base qui ont été utilisées par BORRILL & FERARSTROM (1957-1958) pour mettre en évidence les modifications de diamètre sagittal. Les diamètres transverses dans la partie distale du canal pévien ont augmenté d'environ 0.5 cm dans la plupart des 29 cas ce qui associe l'augmentation du diamètre sagittal du canal pévien donne une augmentation d'environ 20 pour-cent de la surface totale disponible.

REFERENCES

- ANDERSON D. ROBERTS S. M. WILSON P. Relaxation of the pelvic joints in pregnancy. *Surg. Gynec. Obstet.* 58 (1934) 595.
- BARNETT E. Radiology of obstetrics. In: A text book of X-ray diagnosis 4th ed. Vol. V, p. 1. Edited by G. Shanks and P. Kerley. H. K. Lewis and Company Ltd. London 1970.
- BORRILL U. and FERARSTROM I. () The movements of the sacro-iliac joints and their importance to changes in the pelvic dimensions during parturition. *Acta obstet. gynec. scand.* 36 (1957) 42.
- (b) A pelvimetric method for assessment of pelvic mouldability. *Acta radiol.* 47 (1957) 365.
- () Shape and course of the birth canal. A radiographic study in the human. *Acta obstet. gynec. scand.* 36 (1957) 166.
- () Die Umformung des kindlichen Kopfes während normaler Entbindungen in regelrechter Hinterhauptslage. *Geburtsh. u. Frauenheilk.* 18 (1958) 1156.
- (b) Die Umformung des kindlichen Kopfes bei engem Becken. *Geburtsh. u. Frauenheilk.* 18 (1958) 1243.
- LUNDQVIST K. and WESTMAN A. Obstetrik gynecologisk röntgenologi. (In Swedish.) *Nord. Med.* 60 (1958) 1498.
- The mechanism of labor. *Radiol. Clin. N. Amer.* 5 (1967) 73.
- Das weibliche Becken. In: *Gynäkologie und Geburtshilfe*. Vol. II, p. 214. Herausgegeben von O. Kaser et coll. Georg Thieme Verlag, Stuttgart 1967.
- CAMEL M. and VARDY J. The gas or vacuum phenomenon in the pubic symphysis during pregnancy. *Radiology* 66 (1956) 548.
- DUNCAN M. The behavior of the pelvic articulations in the mechanism of parturition. *Dublin Quart. J. med. Sci.* 18 (1854) 60.

- Researches in obstetrics Edinburgh 1868
- CROTHWAITE J F The pelvic articulations J Amer med Ass 49 (1907) 768
- AND OSOOND R B A consideration of the pelvic articulations from an anatomical pathological and clinical standpoint Boston med surg J 152 (1903) 593
- CRITCHFIELD J I Obstetrics 13th ed W B Saunders Company Philadelphia 1965
- HARTLEY J B and LINDLER A S A plan for radiography in obstetrics St Mary's Hospitals Manchester 1966
- HEFELMAN I M and PRITCHARD J A Williams obstetrics 14th ed Appleton Century Crofts London 1971
- HYMAN J and LUNDQVIST A The symphysis pubis in pregnancy and parturition Acta obstet gynec scand 12 (1932) 191
- VON KUTNER O Experiment II anatomische Untersuchungen über die Veränderlichkeit des Beckenraumes Geburtsh Gynäk 1 (1898) 210
- LARSEN Studien über die Funktion der Becken Symphysen während der Geburt (Car medel P ris 35 37 (1862) 558 567) Abstract in Schmidt's Jb ges Med 118 (1863) 301
- I GALLON Expériences sur l' (appendix) 1812 Cited by Abramson coll
- LYNCH W The pelvic articulation during pregnancy labor and puerperium Surg Gynec Obstet 30 (1920) 575
- MACMURDO W Über die Bedingungen des Hervortretens der w rklchen Gelenkspalte auf dem Röntgenbilde Acta radiol 18 (1937) 733
- POUILLET De la rupture des articulations du bassin pendant l'accouchement Lyon méd 1064
- ROBERTS R I Discussion on the physiology and pathology of the pelvic joints in relation to child bearing, A radiological investigation Proc roy Soc Med 27 (1934) 1917
- RUMBLE J C B Cases in the sacro iliac joint in pregnancy J Obstet Gyn Brit Coll 72 (1965) 797
- Moulding of the pelvic outlet J Obstet Gynaec Brit Coll 76 (1969) 817
- SULLIVAN F C Relaxation of the pelvic symphysis during pregnancy and parturition Amer J Obstet Gynec 2 (1870) 361
- THORP D and IRAY W The pelvic joint during pregnancy and labor J Amer med Ass 111 (1938) 1162
- WALCHER C Die Conjugata eines engen Beckens ist keine konstante GröÙe sondern lässt sich durch die Körperhaltung der Frau verändern Zbl Gynäk 13 (1871) 807
- WENIG H The ligament of the sacro iliac joint examined with particular reference to their function Acta anat (Basel) 20 (1951) 201
- The movement of the sacro iliac joint Acta anat (Basel) 23 (1955) 10
- WILLIAMS J I Cases in the symphysis pubis during and following pregnancy Amer J Roentgenol 73 (1955) 403
- YOUNG J Relaxation of the pelvic joints in pregnancy J Obstet Gynaec Brit Emp 47 (1940) 193
- ACAS Mechanism of the pelvic articulations Mth J med Sci Sept 1851 289
- On the symphysis pubis and its contained cavity Mth J med 5 Nov 1851 480

VALUE OF RADIOGRAPHY OF THE REMAINING BREAST FOLLOWING MASTECTOMY FOR CARCINOMA

ALF KOLBENSTVEDT and OLA HELDAAE

A woman who has survived for five years following mastectomy for carcinoma is three to four times more likely to develop a growth in the other breast than a normal woman of the same age (HILGOM 1921). REYNOLDS (1960) reported 160 bilateral tumours during the follow up of 2 671 cases of mammary carcinoma. 93 of these were, however regarded as metastatic. In a twenty year follow up of 1 458 women with mammary carcinoma ROBBINS & BERG (1964) found the annual involvement of the second breast to be reasonably constant and averaged 6 to 7 cases per year per 1 000 at risk. Thus after 10 years nearly 7 and after 20 years nearly 13 per cent of the patients had developed a second primary carcinoma. These authors further stated that while the overall risk of developing mammary carcinoma increases with age the risk of the other breast becoming involved is almost twice as high for a woman under 50 years of age as it is for one over 60. Furthermore the incidence of carcinoma of the second breast in women under 50 years of age is ten times greater than generally in the same age group. Over the age of 70 years however the hazard falls to only twice the general incidence. The risk of a second growth becomes even higher if the first be multiple or a comedo- or an infiltrating lobular carcinoma. ROBBINS & BERG stated that

Table 1

Time interval between the detection of the growths in the two breasts

Years after first operation	N of patients with further primary carcinomas	N of patients with metastases remaining breast
0-1	15	7
1-5	15	2
5-10	11	1
10-20	10	
20-30		
30-40	3	
Total	9	10

Table 2

Number of examinations per patient

N of examination	N of patient
1	51
2	14
3	3
4	1
5	1
Total	3

when a patient attends for follow up examination it is more rewarding from a prognostic point of view to discover an early growth in the remaining breast than to look for distant metastases from the first carcinoma.

The important role of radiography of the female breast in early carcinoma now seems to be widely accepted. One of the main indications for radiography should therefore be the examination of the remaining breast (LECAN 1961; LARSEN & IIVRUD 1967). BYRNIE *et al.* (1962) examined the second breast of 102 women at regular six month intervals for up to seven years. Six had developed primary carcinomas, 5 of which were detected by radiography. MISSENER *et al.* (1963) reported 25 histologically confirmed carcinomas of the other breast following mastectomy, 10 of which were not palpable and detected only by radiography. PICARD & DESIRZ (1958) reported 20 bilateral growths and in 11 of

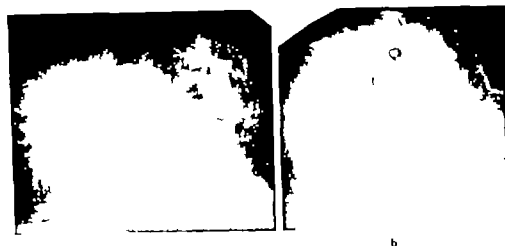


Fig. 1 Both breasts craniocaudal projections. a) Palpable tumour of the right breast b) Two small nonpalpable neoplasms of left breast. Histology indicated bilateral malignancy.

these the second tumour was also discovered by radiography alone. Further experiences in this field are presented in this communication.

Material and Method. The investigation covered 1465 women treated for mammary carcinoma during the four year period 1967—1970. A neoplasm of the other breast was diagnosed in 73 cases. 69 of these were verified by biopsy, 10 of which were histologically metastases, while 59 were considered primary carcinomas. The time interval between the first and second growth appears in Table 1. When this investigation began radiography was not always performed as a routine procedure at follow up but was included once or sometimes more in 53 of these 69 patients. The number of examinations per patient is presented in Table 2. The examinations at regular intervals could have been performed only in a few patients because of the relatively recent introduction of this special technique. The roentgen unit consisted of a Siemens Tridoros 5 modified to yield a low kV with an M tube with wolfram anode and beryllium window. Factors: Kodak M-CEA mammopaque or Ferrania industrial films exposed at 25 to 28 kV 250 mA 2.5—6 s FFD 50 cm.

Results

The examination alone led to biopsy in 15 of the 53 patients (Fig. 1) in 9 out of the 15 patients no tumour being palpable. In the other 6 patients some tissue thickening was palpable but was considered to be benign.



Fig. 2 Remaining breast mediolateral projections. a) Small neoplasm probably malignant. Expectance as the lesion was not palpable. b) 51 months later. The neoplasm is larger. Histology indicated carcinoma.

The average size of the tumours is evident in Table 4. The size is defined as the greatest diameter of the tumour measured after removal. The size in the inoperable group was estimated by clinical examination. If only the operable tumours in stages I and II be considered, those detected by radiography had a smaller average diameter than those that were palpable.

Table 3
Stage distribution of second neoplasm

	Stage I	Stage II	Stages III and IV
Clinically positive	19	5	14
Clinically negative radiographically positive	13	2	
Total	32	7	14

Table 4
Average size of tumour in remaining breast

Clinically positive	4.0 cm (0.5-16)
Clinically positive stages I and II	2.2 cm (0.5-8)
Clinically negative radiographically positive	1.6 cm (0.5-5)



Fig. 3 Remaining breast: cranio-caudal projections. a) No evidence of malignancy. b) One year later. Two small nonpalpable tumours have appeared. Histology indicated carcinoma.

Discussion

Radiography was an indication for biopsy in 28 per cent of the patients despite the fact that it was not performed at regular intervals. Some authors have discovered a still larger number of second growths in a prepalpable state with radiography as a periodic routine procedure (Byrns et coll. 1962).

A first carcinoma of the breast at our centre is if operable treated by radical mastectomy and staged according to the histologic findings in the axillary lymph nodes. A growth of the remaining breast is subjected to simple mastectomy, usually combined with axillary node dissection without removal of pectoral muscles or by conventional radical mastectomy. Its staging is frequently not so exact as that of the first neoplasm.

A comparison of the size of the palpable tumours and those detected by radiography is of no value unless the inoperable ones are excluded: most of these are of course palpable and some are very large in the present material reaching a diameter of 16 cm. Although the average diameter in stages I and II was smaller in the group detected by radiography, some minute tumours although disclosed by palpation were not visible. Radiography was negative in 5 of the 53 examined.

A view of a second breast possibly with a small growth appears in Fig. 2 a. The referring physician could detect no palpable lesion and decided to watch the patient. An examination six months later revealed an increase in the neoplasm which had now become palpable. Histology confirmed the diagnosis. Thus

suggests that possibly malignant tumours should be subjected to biopsy at once even if they are not palpable

A dubious radiographic finding as the only abnormality found may justify an expectant period. With such a finding in a remaining breast, the frequency of bilaterality should be taken into account and weigh heavily in favour of therapeutic or prophylactic mastectomy. The special high risk factors should also be borne in mind (age group, family history, first growth infiltrating lobular carcinoma, comedocarcinoma or multiple primary foci).

The necessity for regular and careful examination of the remaining breast is also well demonstrated in this series by the case illustrated in Fig. 3. Too many patients still come to hospital with advanced disease (40 per cent in stage II or more). The longer the patient lives seemingly free of disease, the more interest should be paid to the second breast and a thorough follow up examination, including radiography, arranged at least every year.

SUMMARY

In 15 (28 per cent) of 53 patients with carcinoma in the remaining breast the second neoplasm was detected by radiography. The operable tumours thus discovered were usually of smaller diameter than those that were palpable. The known high risk factors suggest careful clinical and radiographic examinations of the remaining breast at intervals of not more than twelve months.

ZUSAMMENFASSUNG

Ein Befall der erbliebenden Brust wurde bei 15 (28 %) von 53 Patienten, bei denen eine Mastektomie wegen eines nachgewiesenen Karzinoms vorgenommen worden war, röntgenologisch nachgewiesen. Die dadurch entdeckten operierbaren Tumoren hatten gewöhnlich einen geringeren Durchmesser als die, welche palpabel waren. Die bekannten hohen Risikofaktoren machen sorgfältige klinische und röntgenologische Untersuchungen der verbliebenen Brust in Abständen von nicht mehr als 12 Monaten wünschenswert.

RÉSUMÉ

La radiographie a permis de détecter l'atteinte du sein restant chez 15 malades sur 53 (28 pour cent) qui a été opérée d'une mastectomie avec cancer en place. Les tumeurs opérables ainsi découvertes étaient habituellement de plus petit diamètre que celles qui étaient palpables. Les facteurs de haut risque connus font proposer des examens cliniques et radiographiques soigneux du sein restant à des intervalles ne dépassant pas douze mois.

REFERENCES

- BERG J W and ROBERTS G F Breast cancer Early and late Year Book Medical Publishers
Chicago 1970
- BYRNE R N BRUNCHART L S and GARDNER CORBIN J Postoperative detection of cancer
by periodic mammography of remaining breast Surg Gynec Obstet 115 (1962) 282
- EGAN R L Mammography Charles C Thomas Springfield 1964
- KILOORE A R The incidence of cancer in the second breast J Amer med Ass 77 (1921) 454
- MIRAKIAN M M WITTEN D M and HARRIS L G JR Mammography after mastectomy
J Amer med Ass 191 (1965) 1045
- PICARD J D et DUBREUIL CUREL J P La mammographie a leur diagnostic — résultats
Ann méd chir Cent (Louvain) 14 (1958) 171
- RENNER S Cancer of the breast in women Acta chir scand (1960) Suppl N 266
- ROBERTS G F and BERG J W Bilateral primary breast cancer Cancer 17 (1964) 1501
- TALLE K og LARSEN K Mammografi rontgenologi k blodteknisk undersøkelse v mamma
(In Norwegian) T norske Lægeforen 16 (1967) 1316

DYE DILUTION TECHNIQUE IN THE INVESTIGATION OF RENAL BLOOD FLOW IN SOLITARY CYSTS

JAN GOTHILIN and TORD OLIN

The simple or solitary cyst is a fairly common urologic condition although usually considered harmless. The present investigation was undertaken to determine whether it produces any change in the renal blood flow.

Material and Methods Nine patients with possible renal tumour or cyst referred for angiography were examined by a dye dilution technique (GOTHILIN & OLIN 1970, 1973; OLIN & GOTHILIN 1971). The diagnosis of a simple or solitary cyst was made at nephroangiography and phlebography and by the aspiration of the fluid and the injection of lipiodol.

Results

The diameter of the unilateral cysts in 8 patients (Table 1) varied between 1.5 and 7.1 cm (measurements corrected for magnification) and in the angiographic examinations, except in cases 1 and 2, formed a part of the contour of the kidney.

Table 1

Renal blood flow and related parameters in kidneys with solitary cysts

Case	Age	Sex	S	RAD	RBF	RBF/m	VV	VR	MTT	Cyst (cm)
1	5	F	L	4.7	439	271	74	21	10.1	1 × 1.5
2	70	M	R	5.3	380	190	58	27	9.1	2 × 2 Cystic carcinoma of contralateral kidney
3	4	M	L	6.8	400	194	53	15	7.9	Two cysts both 2 × 2
4	63	M	L	6.0	234	142	37	30	8.8	2.7 × 2.7
5	79	F	R	4.5	291	151	38	20	7.8	3.4 × 4.1
6	67	F	L	3.8	208	115	48	37	15.7	4.2 × 4.2
7	55	F	R	3.8	214	130	3	45	9.9	4.8 × 4.8
8	64	M	R	6.4	278	140	55	34	11.9	5.5 × 5.5
9	68	F	L	5.5	177	111	29	63	9.8	7.1 × 7.1
				5	9	8	9	9	9	
Mean				5.2	294	160	47	37	10.1	
SD				1.1	93.6	50.1	14.1	17.9	2.4	
SE				0.4	31.2	16.9	4.7	6.0	0.8	
t				14.8	9.4	9.5	10.1	6.3	12.5	
S	Localisation of kidney									
RAD	Diameter of renal artery									
RBF	Renal blood flow (ml/min)									
RBF/m	Renal blood flow (ml/min/m ² body area)									
VV	Vascular volume (ml)									
VR	Vascular resistance (peripheral resistance units)									
MTT	Mean transit time (seconds)									

Case 3 had two cysts in one kidney each 2.0 cm in diameter the radius of a sphere of the calculated volume was plotted in the diagrams. Case 1 with the kidney with the smallest cyst had a normal renal blood flow/m² body area (normal RBF/m² = 268 ml/min SD = 63.2 SE = 12.6). The vascular volume (normal 66 ml SD = 14.5 SE = 2.9) and the vascular resistance (normal 20 peripheral resistance units SD = 4.8, SE = 1.0) were also normal. No deviations in the parameters of the contralateral kidney were recorded.

The renal blood flow/m² of body area was reduced in cases 2 to 9 with a tendency to a more marked reduction in larger cysts (Fig. 2). A rise in vascular resistance (Fig. 3) and a decrease in vascular volume occurred with increasing cyst size (Table 1). The renal blood flow was also measured in the contralateral kidney in 6 patients and the same values as in the cystic kidney although slightly less marked (Table 2) were evident. Good linear correlation ($r = 0.9$) between



Fig. 1. Angiography of the left kidney of case 6. a) Arterial phase. Cyst (b) diameter of about 4 cm; the upper half of the kidney with displacement of arteries. b) Nephrographic phase.

the two sides as regards renal blood flow and vascular resistance. (Figs 4, 5, 6) was present. Urography demonstrated normal excretion of contrast medium but deformity due to the cyst and diminished renal size. The angiograms of the cases with increased vascular resistance disclosed reduced cortical thickness and tortuous and narrow arteries. No cortical scars were evident. When the vascular resistance was markedly increased the angiographic appearances resembled those of so called nephrosclerosis.

Discussion

The term simple cyst appears preferable to solitary cyst to describe an isolated sac filled with serous fluid. The term solitary cyst will however be used in this communication as it is prevalent in the world literature and also employed in



Fig 2

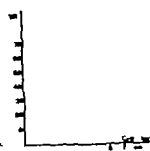


Fig 3

Fig 2 Renal blood flow (RBF) related to the size of the cyst

Fig 3 Vascular resistance (VR) related to the size of the cyst

Table 2

Renal blood flow, vascular volume and vascular resistance in bilaterally resected patients

Case	RBF		VV		VR	
	Cyst	Contralat	Cyst	Contralat	Cyst	Contralat
1	439	444	74	67	21	20
2	380	—	58	—	27	—
3	405	485	53	56	15	13
4	254	—	37	—	3	—
5	294	—	38	—	20	—
6	208	206	48	41	57	5
7	214	319	35	46	42	30
8	278	258	55	32	54	6
9	177	220	29	30	63	51
	9	6	9	8	9	8
Mean	294	319	47	49	37	39
SD	93.6	170.3	14.1	12.8	17.9	20.2
SE	31	49.3	4.7	5.2	6.0	8.3
t	9.4	6.5	10.1	3.3	6.3	4.6

Cyst kidney with cyst

Contralat Contralateral kidney

RBF Renal blood flow (ml/min)

VV Vascular volume (ml/min)

VR Vascular resistance (peripheral resistance units)

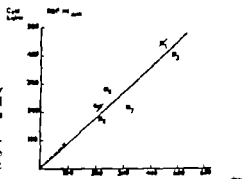


Fig. 4. Relation between the renal blood flow (RBF) of the kidney with solitary cysts and that of the contralateral kidney. The numbers of the squares correspond to the case numbers. The dotted line represents regression coefficient of 1.0 and the full line that of the blood flow of the contralateral kidney to that of the cystic kidney.

urologic practice FAHRMAN (1968) stated that the incidence of solitary cysts is about 1 in 3 500 subjects of an average age of about 50 years.

It is still not clear whether the cysts are acquired or congenital (FREUSON 1960). HEPPLER (1916) produced solitary cysts experimentally in rabbit kidneys by ligating a tubule and occluding the vascular supply to the papilla of the area.

The cysts contain a clear serous fluid with a specific gravity of 1.002 to 1.010 but no urine. Most grow slowly over a period of years although a few develop rapidly. They may lie in the cortex or extend to a calyx or to the pelvis of the kidney. As they increase in size they replace the kidney tissue and finally destroy the cortex by growth and pressure. Solitary cysts are frequently asymptomatic and are discovered accidentally at urography. Hypertension in connection with cysts is mentioned by KREUTZMANN (1947) but common experience favours the opinion that hypertension is not a typical feature. The blood pressure was normal in all the present cases.

BJERLE *et coll.* (1971) measured the pressure in renal cysts. This varied from -1 mm Hg to $+32$ mm Hg in solitary cysts while the creatinine in ml/100 ml serum was normal. These authors reported no correlation between the size and the internal pressure of the cysts. In polycystic disease the pressure in adjacent cysts differed and the authors therefore concluded that the intracapsular pressure had little influence upon that in the individual cyst. When multiple cysts existed a positive correlation between the cystic pressure and the creatinine in the serum was evident.

The mechanism underlying the relationship between the diminished blood flow, reduced vascular volume and increased vascular resistance in one kidney and the occurrence and size of cysts in the contralateral kidney is not obvious. A cyst will compress the surrounding parenchyma to a certain degree and thereby impair the circulation. If the renin-angiotensin mechanism be activated both

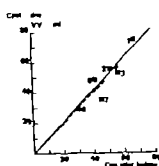


Fig 5

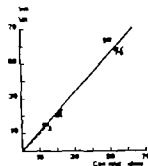


Fig 6

Fig 5 Relation between the vascular volume (VV) of the kidneys with solitary cysts and that of the contralateral kidney. The numbers of the squares correspond to the case numbers. The dotted line represents regression coefficient of 1.0 and the full line that of the blood flow of the contralateral kidney to that of the cystic kidney.

Fig 6 Relation between the vascular volume (VV) of the kidney with solitary cysts and that of the contralateral kidney. The numbers of the squares correspond to the case numbers. The dotted line represents regression coefficient of 1.0 and the full line that of the blood flow of the contralateral kidney to that of the cystic kidney.

kidneys will be influenced as in the present material. The conception of such a mechanism may perhaps be a little far fetched as the systemic blood pressure was normal in all cases even when the cyst was large and the renal blood flow markedly reduced bilaterally. A permanent decrease in the flow occasioned by a nerve mechanism is not especially convincing either. Another possibility is the existence of a primary condition of the kidney to which the solitary cyst is a sign only of increasing disease. The changes demonstrated angiographically in cases 8 and 9 resembled those of so-called nephroscleroses. Against the theory of primary renal disease is the fact that most solitary cysts are unilateral as in the present material.

Animal experiments (HEPLER 1946) have demonstrated that it is possible to produce a cyst by obstructing a tubule. The possibility of a tubule being isolated by shrinkage of the kidney increases with progressing nephrosclerotic changes. No arterial changes in the small cysts of the present material were however evident.

The reason for the correlation between the size of the cysts, the decrease in the renal blood flow and vascular volume and the increase in the vascular resistance is thus obscure. Further investigations in this field with control of the renal blood flow and related parameters before and after puncture have consequently been initiated.

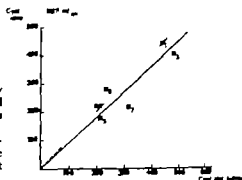


Fig 4 Relation between the renal blood flow (RBF) of the kidney with solitary cysts and that of the contralateral kidney. The numbers of the squares correspond to the case numbers. The dotted line represents regression coefficient of 1.0 and the full line that of the blood flow of the contralateral kidney to that of the cystic kidney.

urologic practice FAHRMAN (1968) stated that the incidence of solitary cysts is about 1 in 3 500 subjects of an average age of about 50 years.

It is still not clear whether the cysts are acquired or congenital (FREUSON 1960). HEPLER (1946) produced solitary cysts experimentally in rabbit kidneys by ligating a tubule and occluding the vascular supply to the papilla of the area.

The cysts contain a clear serous fluid with a specific gravity of 1.002 to 1.010 but no urine. Most grow slowly over a period of years although a few develop rapidly. They may lie in the cortex or extend to a calyx or to the pelvis of the kidney. As they increase in size they replace the kidney tissue and finally destroy the cortex by growth and pressure. Solitary cysts are frequently symptomless and are discovered accidentally at urography. Hypertension in connection with cysts is mentioned by KREUTZMANN (1947) but common experience favours the opinion that hypertension is not a typical feature. The blood pressure was normal in all the present cases.

BJERLE *et al.* (1971) measured the pressure in renal cysts. This varied from -1 mm Hg to $+32$ mm Hg in solitary cysts while the creatinine in mg/100 ml serum was normal. These authors reported no correlation between the size and the internal pressure of the cysts. In polycystic disease the pressure in adjacent cysts differed and the authors therefore concluded that the intracapsular pressure had little influence upon that in the individual cyst. When multiple cysts existed a positive correlation between the cystic pressure and the creatinine in the serum was evident.

The mechanism underlying the relationship between the diminished blood flow, reduced vascular volume and increased vascular resistance in one kidney and the occurrence and size of cysts in the contralateral kidney is not obvious. A cyst will compress the surrounding parenchyma to a certain degree and thereby impair the circulation. If the renin-angiotensin mechanism be activated both

ACCURACY OF ANGIOGRAPHY IN THE DIAGNOSIS OF CARCINOMA OF THE PANCREAS

U. TYLEN

The incidence of carcinoma of the pancreas is rising (BEALL et coll 1970 KRAVY 1970). At the same time the results of surgery in this type of malignancy are poor (GLENY & THORBJARNARSSON 1964 BEALL et coll 1970 FEDUSKA et coll 1971 POPE & FISCH 1971) due to the fact that early symptoms are absent or uncharacteristic. The patient usually fails to seek medical advice until late when jaundice has developed or pain has become intractable (KLEINTRUP 1966 CHILD & FREY 1966 BEALL et coll) the tumour because of local and distant spread is then seldom operable.

Angiography has during the past decade become increasingly used in the diagnosis of pancreatic disease. It is however doubtful if it is possible even by this method to make the diagnosis early enough to insure successful removal of a new growth of the pancreas. Many surgeons therefore believe that there is no place for angiography in pancreatic disease. All investigators of angiography in carcinoma of the pancreas however affirm that the diagnosis is possible only the incidence of vascular changes and thus the degree of accuracy is controversial (LUNDERQUIST 1963 MEANEY & BOUNOCORE 1965 ROSCH & BREIT 1963 HERNANDEZ et coll 1967 NEBERAR & POLLARD 1967 NUSBAUM et coll

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1967 SAMUOVS et coll 1967 WEISSLEDER et coll 1967 BOGASTEIN et coll 1969 FREDEN et coll 1969 TAVERNIER et coll 1969 BOIJSEN 1970, LECTNER et coll 1970 OLSSON 1970 REUTER et coll 1970 BUEHLER et coll 1971, SUZUKI et coll 1971)

The purpose of the present investigation therefore was to evaluate the diagnostic accuracy of angiography in a large series of patients with verified carcinoma of the pancreas. In addition, the cause of incorrect preoperative diagnosis either negative or positive, was to be determined.

Material and Methods The present investigation covered 134 patients examined by angiography during the years 1959 to 1971 i.e. from the time it was first used by us in the diagnosis of pancreatic carcinoma. The clinical diagnosis in 116 patients included a few cases with carcinoma of the distal part of the common bile duct or of the papilla of Vater in which the differentiation was not clinically or pathologically clear (The cases reported by LUNDERGREN 1965 are included). The diagnosis was verified post mortem in 48 patients and by surgical exploration in 66 in 41 of whom biopsy was performed. In one patient the verification was provided by biopsy of a subcutaneous lymph node metastasis in another by percutaneous fine needle biopsy of the tumour directed by the findings at angiography. The growth involved the head of the pancreas in 87 patients the body in 21 and the tail in 8 patients. This distinction is somewhat arbitrary since large tumours often involved more than one part of the gland but was considered practical in analysing the angiographic findings. The neoplasms have therefore been referred to the part of the pancreas mainly involved as adjudged from the findings at operation or post mortem examination.

A correct preoperative diagnosis of carcinoma of the pancreas at angiography was made in 79 of the 116 patients: the diagnosis was pancreatitis in 11 and postoperative changes in 3 patients. No pathologic changes indicating malignancy were evident in 23 patients.

A preoperative angiographic diagnosis of carcinoma made in an additional 18 patients, proved incorrect at operation. Inflammatory changes in the pancreas were present in 5 of the patients, another had biliary tract disease and one had stenosis of the papilla of Vater: no changes were evident in 8 patients. No verification was obtained in 3 patients and clinical evidence of carcinoma of the pancreas has not developed.

Examination of both the coeliac axis and superior mesenteric artery by simultaneous or sequential injections was performed in 103 patients. The superior mesenteric artery only was injected in 4 instances due to stenosis of the coeliac axis: a further 25 patients having examinations only of the coeliac axis.

Table

Angiographic findings in 116 patients with carcinoma of the pancreas

	Part mainly involved by tumour			Total
	Head	Body	Tail	
Encasement of large arteries	28	18	8	54
Encasement of small arteries	71	17	5	93
Regular stenosis	22	9	4	35
Tumour vessels	59	11	5	75
Displacement of arteries	22	7	2	31
Involvement of intestinal arteries	6	7	1	14
Arterial spasm	20	1	—	21
Tortuous pancreatic arteries	36	3	4	43
Inflammatory changes in pancreatic arteries	15	—	—	15
Hypervascularization	38	3	5	46
Hypovascularization	7	—	—	7
Venous lesions	32	17	8	57
Occlusion	7	16	7	30
Compression	25	3	2	32
Enlarged gallbladder	58	2	—	60
Total	67	21	8	116

The information thus obtained in 18 patients was considered insufficient and catheterization of the common hepatic artery was performed. The splenic and gastroduodenal arteries were selectively catheterized in two patients respectively.

Pharmacologic agents such as norepinephrine and vasopressin were used in 36 patients in order better to demonstrate the vessels of the pancreas. Bradykinin was utilized in 32 patients in order to improve the demonstration of the large veins.

The angiograms were examined in retrospect. The findings were correlated with the preoperative diagnosis and with those at operation. Special consideration was also directed to the appearances in patients in whom resectional surgery was attempted. This will be reported in another paper.

Results

Angiographic findings in 116 patients with verified carcinoma of the pancreas

The diagnosis of carcinoma of the pancreas may be based on the demonstration of the irregular encasement of arteries and the presence of tumour vessels. Encasement is evident as stenotic changes, the outlines of the arteries typically appearing



b



FIG. 1. Male aged 63 with carcinoma of the pancreas. No operation. Diagnosis provided by percutaneous fine needle biopsy. a) Irregular encasement of splenic artery and small pancreatic vessels. Collateral circulation to the spleen through right gastroepiploic artery. Displacement of the pancreas to the left. b) Encasement of the main stem of superior mesenteric artery. Occlusion of the portal. Rich enough collateral circulation to the hilum of the liver.

irregular. It was demonstrated in 103 patients (Table). Large arteries i.e. the coeliac axis, the superior mesenteric, hepatic, splenic or gastroduodenal arteries were encased in 54 patients. In 44 of these encasement of small arteries i.e. the pancreatic arcades, the dorsal pancreatic, transverse pancreatic arteries or



Fig 2 Woman aged 53 with inoperable carcinoma of the tail of the pancreas overlooked preoperatively. Irregular encasement of splenic artery in hilum of the spleen (\rightarrow) proximal to high short regular stenosis (\leftarrow) Tumour caecum



Fig 3 Man aged 57 with operable carcinoma of the head of the pancreas. Encasement of gastroduodenal artery and pancreatic arcades. Distension of gallbladder

the arteries to the tail of the pancreas was also demonstrated. Two or more large arteries were encased in 23 patients (Fig 1) only the splenic artery in 6 (Fig 2) and only the gastroduodenal artery in 20 patients (Fig 3). Encasement of small arteries only was evident in 49 patients (Figs 4-5).

Stenotic changes different from irregular encasement and perhaps not caused by malignancy were evident in 35 patients; these were smooth, regular and slight. Only one artery was usually affected, but in 11 instances changes were recorded in two or more arteries, usually in the splenic and hepatic arteries. In 32 patients they were associated with irregular encasement of large or small arteries (Fig 2) in only 3 of whom coexistent irregular encasement was absent. Of these one had a pseudocyst, one inflammatory changes (Fig 6) and in one the technical quality did not permit evaluation of the finer detail.

Wide invasion of retroperitoneal structures as evidenced by encasement of the coeliac axis was present in 10 patients. All had large inoperable tumours, sometimes with involvement of the left gastric artery (1) and of the renal arteries (2). A spread to the root of the mesentery was indicated in 9 patients by encasement of the main stem of the superior mesenteric artery (Fig 1). Involvement also of the branches of this artery was demonstrated by encasement and tortuosity in 8 patients (Fig 7) and increased tortuosity of the middle colic artery alone in 5 patients.



Fig. 4. Man aged 78 with small carcinoma of the head of the pancreas. Encasement of inferior pancreaticoduodenal artery and branches. Tumour vessels. Distension of gallbladder.



Fig. 5. Woman aged 74 with an operable carcinoma of the head of the pancreas. Occlusion of superior pancreaticoduodenal artery (→). Tumour vessels.

Tumour vessels are newly formed, irregular, tortuous small vessels. They may at angiography be difficult to differentiate from small arterial branches with encasement. They were demonstrated in 75 patients and in 6 patients were the sole indications of malignancy (Fig. 8). Thus 109 of the 116 patients had encasement with or without tumour vessels.

Displacement of arteries was evident in 31 patients. Medial displacement of the gastroduodenal artery, usually associated with encasement and linking, was evident in 10 patients (Fig. 3). In 7 patients, all with a growth of the head of the pancreas, the gastroduodenal artery was stretched and laterally displaced. In another 9 patients the entire vasculature of the pancreas, including the gastroduodenal artery, was displaced to the left and cranially. This type of displacement was always associated with large tumours involving the entire gland and surrounding tissues. Extensive arterial encasement was demonstrated in addition (Fig. 1). A similar type of displacement was present in 4 patients with enlargement of the liver but without extensive arterial encasement however. The left gastric artery in one patient was stretched by an expansive lesion in the body and tail of the pancreas.

Tortuous arteries in the pancreas were evident in 45 patients in 5 of these probably due to collateral circulation because of stenosis of the coeliac artery.



Fig 6 Woman aged 39 th operable carcinoma of the head of the pancreas \ encasement of arteries nor tumour cowl Arteries in tail of the pancreas tortuous th irregular lumen suggesting pancreatitis

The tortuous vessels were often located in the body and tail, distal to the carcinoma when this was situated in the head

Arterial changes usually regarded as secondary to pancreatitis were evident in 15 patients with carcinoma of the head of the pancreas thus the lumen of the small pancreatic arteries was slightly irregular with alternating dilatations and narrowings The changes were frequently associated with increased tortuosity and were always located distal to the growth in the body and tail of the pancreas (Fig 6)

Hypovascularization was present in 46 patients and was sometimes located in the proximity of the involved area and sometimes distal to it Early venous filling was never demonstrated and draining veins were evident in only 2 patients Hypovascularization was noted also distally in 7 patients

Venous lesions were observed in 57 patients Occlusion was diagnosed when complete obstruction in a vein was present or when a vein was invisible and collateral circulation was evident Compression was diagnosed when the vein was deformed from the outside but when complete obstruction was not demonstrated Delayed emptying of a vein was also regarded as indicating compression Of 29 patients with carcinoma of the body and tail of the pancreas 23 had occlusion of the splenic vein one of the portal vein (Fig 1) and 5 had compression of the superior mesenteric vein Compression alone of the superior mesenteric or splenic veins was evident in another 2 patients On the other hand with a growth in the head of the pancreas the splenic vein was occluded in 6 and the superior mesenteric vein in one patient Compression of the veins was more common and was present in the confluent parts of the splenic and



Fig. 7. Man aged 75 with inoperable carcinoma of the head and body of the pancreas. Liver metastases and invasion of the root of the mesentery. Encasement of main stem of superior mesenteric artery and branches to jejunum.

superior mesenteric veins in 9 patients, in the splenic vein in 8, the superior mesenteric vein in 4, and the portal vein in 4 patients. The splenic vein was invisible or too poorly filled to permit evaluation in 6, and the superior mesenteric vein in 11 patients of the series. This means that the incidence of venous lesions may have been even higher. Further angiographic details appear in the Table.

Percutaneous fine needle biopsy was performed in 5 patients at the same session as the angiographic examination with the catheters in place for orientation. In 3 of these, all with extensive growths, the angiographic diagnosis could be confirmed. In a further 2 patients with smaller neoplasms no specimen was obtained.

Findings in 30 patients in whom only a retrospective diagnosis of carcinoma was made. Irregular stenotic arterial changes were reported preoperatively in 5 patients; these were not attributed to carcinoma of the pancreas, however, but to atheromatosis in 2 and to chronic pancreatitis in one patient. In the remaining two patients examined during the early years of angiography conclusions of the stenotic changes were not drawn. The retrospective revelation of



Fig. 8. Man aged 69 with operable carcinoma of the head of the pancreas. Incorrect negative diagnosis at primary evaluation. Fine tumour vessels around gastroduodenal artery (→). No arterial encasement.

tumour vessels although scanty in 4 patients made the diagnosis obvious. The diagnosis of pancreatitis was made preoperatively in another 8 patients in this group. They had previously been thoroughly examined (TYLEN 1973). Clinical evidence of pancreatitis was present in only 2 of these expansive lesions, probably pseudocysts, were angiographically diagnosed in both cases because of arterial displacement. At operation large carcinomas with cystic degeneration were disclosed. In retrospect it was noticed that the walls of the cystic lesions were unusually thick and highly vascular and encasement of small arterial branches was evident. The angiographic diagnosis of pancreatitis was verified at operation in another patient who died a few months later but in whom autopsy disclosed carcinoma of the pancreas. Retrospective examination of the films revealed irregular encasement of the splenic artery and venous occlusion findings that were reported preoperatively as suggesting chronic pancreatitis. concomitant inflammatory vascular changes in small intrapancreatic arteries were also demonstrated. In another patient in whom pancreatitis was diagnosed arterial changes suggestive of pancreatitis in the body and tail of the pancreas were evident. Retrospective examination also disclosed encasement of arteries and tumour vessels in the head of the pancreas.



Fig 9. Man aged 58 with abdominal pain. Pancreatic arcades slightly irregular. Diagnosis of carcinoma made preoperatively and at operation. Pathologic examination of specimen normal pancreatic



Fig 10. Man aged 70 in need for melectomy. Marked irregularity of branch of pancreaticoduodenal arcade. Retrograde examination of head of pancreas. Operation light and easy. Post mortem examination normal pancreas.

Incomplete examinations or examinations of poor technical quality may have contributed to the fact that the growth was overlooked in the remaining 14 patients with an incorrect preoperative diagnosis of pancreatitis.

The angiographic evaluation was particularly difficult in 3 patients in whom at operation before angiography a pseudocyst in the head of the pancreas, an atypical duodenal ulcer, and a stricture at the papilla of Vater respectively had been found. The angiographic examinations were performed because the diagnosis was considered uncertain. Marked vascular changes were demonstrated at angiography, but they were regarded entirely as postoperative. The subsequent course of the disease revealed carcinoma of the pancreas. Retrospectively the changes were considered more marked than might have been expected after only exploration or a shunting operation. Enhancement was evident in all three patients as were tumour vessels.

No abnormal findings referable to the pancreas were reported preoperatively in 14 patients. The tumours at operation were large in 8 of these patients; the

size being described as resembling a fist or a tennis ball. With our present knowledge encasement of large as well as of small arteries, tumour vessels and venous lesions could be demonstrated retrospectively in 3 of the patients (Fig. 2). The other 5 patients presented encasement of small arteries and 2 of these also had tumour vessels. The changes, although small, were confirmed retrospectively. Technical factors probably influenced the evaluation in 2 of the patients, in one of whom an enlarged liver considerably displaced the pancreatic vasculature.

Tumours 1 cm to 4 cm in diameter were evident at operation in 6 patients, in 4 of whom, in spite of their small size, encasement of small arteries in the head of the pancreas was demonstrated. In addition, tumour vessels were revealed in 4 patients, in 2 of whom as the only pathology (Fig. 8). In one of the latter only the superior mesenteric artery was injected due to stenosis of the coeliac artery. This artery filled via collaterals around the head of the pancreas, a fact which complicated the evaluation since they were wide and tortuous.

Thus in this group, changes characteristic of carcinoma of the pancreas were reported in 9 patients. However, they were attributed to previous operations in 3, to atheromatosis in 2, to pancreatitis in 2, and no conclusions were drawn from the findings in 2 patients. Malignant changes were present but unobserved in 17 patients, although in 3 of these they were extensive. Poor technique contributed to incorrect negative diagnosis in 4 patients.

Findings in 7 patients in whom not even retrospectively a diagnosis of carcinoma was possible. The preoperative diagnosis was pancreatitis in 2 patients, while in the remaining 5 patients no abnormalities in the pancreas were reported. In none of the 7 patients was irregular encasement of arteries or tumour vessels evident retrospectively. At operation a small operable tumour was present in 3 patients. In one of the latter angiography revealed smooth slight stenosis of the splenic artery and the small vessels in the body and tail of the pancreas had irregularities in the lumen with alternating narrowings and dilatations. In addition the splenic vein was compressed (Fig. 6). Few changes were evident in the remainder: localized hypervascularization of the head in one patient, and tortuous vessels and an enlarged gallbladder in the other.

The tumour at operation was larger in 3 other patients. In spite of this, only slight hypervascularization and a few tortuous vessels corresponding to the size of the mass were demonstrated in 2 of these patients. The third patient had slight smooth stenosis of the splenic artery, displacement of the left gastric artery and occlusion of the splenic vein, indicating an expansive lesion of the tail of the pancreas. Further details were not possible to evaluate since the technical quality of the examination was poor because the catheter receded to the aorta at the injection of the medium. The seventh patient, in whom a retrospective

diagnosis was not possible, and a long history of pancreatitis. A pseudocyst was diagnosed angiographically based on displacement and stretching of the pancreatic arcades and occlusion of the splenic vein. Operation confirmed the pseudocyst but also revealed carcinoma of the head of the pancreas.

Findings in 18 patients with incorrect positive diagnosis of carcinoma of the pancreas. Patients in whom the diagnosis of carcinoma was made but in whom operation disclosed the origin of the tumour to be adjacent to the pancreas are here excluded. The most common findings, upon which the incorrect diagnoses were based, were tortuous and irregular arteries in 12 patients; in 4 of these the changes were interpreted as due to encasement. Eleven patients were operated upon and a normal pancreas was revealed in 4 and pancreatitis in 4 patients. One patient had stones in the common bile duct and another stenosis of the papilla of Vater as indicated by dilatation of common bile and pancreatic ducts at operative cholangiography. In one patient carcinoma of the pancreas was considered probable at operation and pancreaticectomy performed. The pathological examination, however, disclosed a normal pancreas. The patient was still alive 3 years postoperatively although with signs of malabsorption (Table 9). The patients not operated upon have not developed signs of malignant disease.

Retrospective analysis of the films revealed marked and localized vascular irregularities in 4 patients (Fig. 10). The diagnosis of carcinoma was therefore again suggested. Operation disclosed inflammatory changes in the head of the pancreas in 3 patients; the other had a normal gland. More generalized changes in the pancreas were apparent in one patient. The changes were similar to those frequently demonstrated in pancreatitis, which was also the operative diagnosis. In the remaining patients the tortuosity and slight irregularity of the vessels were less marked and could be attributed to normal variations.

Tumour blush or tumour vessels were reported in 5 patients. At operation the pancreas was normal in 3 and in another patient in whom displacement and smooth stenosis of the gastroduodenal artery were also evident, a pseudocyst of the pancreas was discovered. The fifth patient had repeat angiography a few months later with normal findings.

It appeared in retrospect that the incorrect diagnosis was caused by misinterpretation of marked hypervascularization of the duodenum in 4 of the patients. The patient with a pseudocyst had, however, within a small area adjacent to it very markedly deranged vessels that could not with certainty be differentiated from tumour vessels.

Displacement of arteries was diagnosed in 6 of the 18 patients. Vascular displacement was in one patient the sole finding upon which the diagnosis of carcinoma was based. Exploration was not performed but she is still alive 7 years

after angiography which rules out carcinoma of the pancreas. Retrospectively displacement could be accepted in only one case that with the pseudocyst of the pancreas. The vascular deviations in the other cases were considered to be within normal limits.

A retrospective diagnosis of carcinoma was thus made in 5 patients, 4 of whom were diagnosed as having pancreatitis at operation. The diagnosis was made because of marked vascular irregularities which were strictly localised. With the exception of generalized changes compatible with pancreatitis in one patient the reported changes were considered to be within normal limits in the remaining

Discussion

A proper technique of examination in the angiographic diagnosis of pancreatic disease is of extreme importance. There is however no single method that is better than any other in every instance: the technique must be adjusted to the findings in the individual patient and the examination must proceed until malignancy is confirmed or eliminated. Examination of both the coeliac and the superior mesenteric arteries is necessary for full evaluation of the pancreatic vasculature. The catheterizations and roentgenographic technique must be beyond reproach: the use of pharmacologic agents may be required.

Knowledge of the anatomy of the pancreatic vessels makes it possible to differentiate the pathologic findings from the many normal variations. The difficulties are emphasized even more when differentiation between inflammatory and malignant disease is the point: this differentiation can be made usually only by those with great personal experience of angiography in pancreatic disease.

The angiographic diagnosis of carcinoma of the pancreas necessitates the demonstration of irregular encasement of arteries and of tumour vessels. Previous investigators agree that encasement is common although the reported frequencies vary (MEANEY & BLONOCOME 1958; ROSS & BREY 1960; LUDIN *et coll.* 1966; NENFAR & POLLARD 1967; WEISSLEDER *et coll.* 1968; FREDENS *et coll.* 1970; TAVERNIER *et coll.* 1971) in large materials however the incidence is about 75 per cent (LUNDERQUIST, POOKSTEIN *et coll.* 1972). Encasement was present in 103 out of 116 patients (88 per cent) of the present material. Encasement of large arteries is typically irregular (Fig. 2) but smooth stenoses also occur (POOKSTEIN *et coll.* 1972). Smooth regular stenoses in extrapancreatic arteries may be suggestive of pancreatitis however (HERNANDEZ *et coll.* 1970; REUTER *et coll.* 1969; BOJSEN & TILLY 1972; TILLY & ARNOLD 1973). Such stenoses were evident in 35 patients but in only 3 were they present without concomitant irregular encasement: in these 3 the angiographic diagnosis of carcinoma was then missed since tumour vessels were absent.

Most authors report low incidence of tumour vessels in carcinoma of the pancreas (MEANEY & BUONOCORE, NEHESAR & POLLARD, WEISSLEDER *et coll.*, LECHNER *et coll.*, BUCHELER *et coll.*). This may be due to poor vascularization of adenocarcinoma of the pancreas. LUNDERQUIST and BOOASTEN *et coll.* observed tumour vessels in almost 60 per cent of their cases. This is in accordance with the findings in our material. An extremely good technique is necessary for the demonstration of small and scanty tumour vessels and by further improvement in the technique they will probably be demonstrated more frequently.

Displacement of arteries is another finding often reported. Displacement, however, is particularly difficult to evaluate because of the great normal variations. Since carcinoma infiltrates rather than displaces surrounding tissues, displacement of arteries should not be expected frequently (OLSSON). It was present in 31 patients in this series, however. Medial or lateral displacement of the gastroduodenal artery was commonly encountered. In 3 patients all with long histories of pancreatitis the lateral displacement was marked, the pancreatic arcades in addition being stretched and the diagnosis was therefore pseudocyst. At operation, however, the pseudocyst in one patient proved to be secondary to carcinoma, an uncommon complication (BUCK & FLETCHER 1972). The other patients had large carcinomas with cystic degeneration and, in retrospect, encasement of small arteries. A particular type of displacement of the whole gland to the left was noted in 9 patients all with extensive malignant spread into surrounding tissues (Fig. 1). A similar type of displacement has been reported in chronic pancreatitis due to retroperitoneal adhesions (BOIJSEN & TYLEN 1972). In the presence of carcinoma of the pancreas however extensive arterial encasement appears always to exist and differentiation should therefore be possible.

Changes such as encasement or increased tortuosity in arteries feeding the small bowel were evident in 14 patients in the material. Increased tortuosity with slightly irregular lumen of the middle colic artery may also be demonstrated in chronic pancreatitis (BOIJSEN & TYLEN). This alone, therefore, does not indicate spread of the growth to the mesentery. However when intestinal arteries and even the main stem of the superior mesenteric artery are irregularly encased it is clear that the root of the mesentery has been involved (Fig. 7).

Inflammatory changes surrounding and distal to carcinoma of the head of the pancreas are often present at operation (GLEN & THORBJARNARSON, KLEINLUF). This corresponds well to the findings in 15 patients in this material of inflammatory changes in the vessels of the body and tail of the pancreas. These consisted of increased tortuosity and lumen variations (Fig. 6) and were similar to those described in pancreatitis (REUTER *et coll.* 1969, TYLEN & ARNESEN). The changes must be differentiated from tumour vessels, which, however, are more

irregular and deranged. The latter are in addition, usually strictly localised unless the growth is extensive when arterial encasement also becomes evident. The inflammatory changes on the other hand, usually involve the whole gland. If therefore such changes localised to the body or tail of the pancreas are apparent carcinoma of the head is possible and the examination should proceed until this can be eliminated (BOYSSON 1971).

Arterial spasm, tortuous pancreatic vessels and abnormalities of the vascularisation were frequently noted in the present series (Table). Arterial spasm is often observed in pancreatitis and has been put down to increased sensitivity of the arterial wall to the hypertonic contrast medium (TILLY & ARNESEN). A similar mechanism may be responsible also in pancreatic carcinomas since the latter are often surrounded by a zone of inflammation. When evaluating the vascularisation of the pancreas the great number of normal variations must be borne in mind. Hypervascularisation was common in this material but unless combined with other changes characteristic of malignancy this affords little help in the diagnosis. The same holds for increased tortuosity of the pancreatic vessels.

The reported incidence of venous lesions in carcinoma of the pancreas is usually about 25 per cent (NEBERAR & POLLARD; BOOKSTEIN *et coll.*; FREDEN *et coll.*; LUGHESE *et coll.*; BUCHELER *et coll.*). TAVERNIER *et coll.* however reported compression of the veins in 9 and occlusion in one of their 11 patients and BURANASTRI & BAUM (1972) described venous involvement in 46 of their 47 patients. Venous lesions were present in 57 of the 116 of the present material. Venous occlusion may be diagnosed at angiography with a high degree of accuracy if an appropriate technique is used. Occlusion does not necessarily mean thrombosis: it indicates only that the circulation in the vein is completely blocked. Slight compression on the other hand, may be overlooked especially if it affects the veins in a straight dorsal direction and deformation of their outlines is therefore obscured. The lesions were more frequently encountered in growths of the body and tail than in those of the head. This may be due to the fact that signs of a carcinoma of the former parts appear later and that the mass is then larger (MILLER *et coll.* 1951). On the other hand the body and tail are more intimately associated with in particular the splenic vein. Moreover growth of the head produced venous involvement more often by compression than by occlusion. It should however be realised that the high incidence of venous involvement in pancreatic disease is simply a result of the fact that the large veins pass close to the gland and that since they are soft and easy to compress they are susceptible to pressure from every expansive lesion in the surroundings whether of benign or malignant nature.

Poor technical quality or insufficient knowledge of anatomic variations was

responsible for many of the incorrect diagnoses in this material. The technique has improved with time however and more experience of the findings in carcinoma of the pancreas and pancreatitis has led to errors occurring more rarely. The angiographic diagnosis of large carcinomas is seldom difficult but when the vascular changes are small and localized difficulties may arise. Since the prognosis in this condition is extremely poor and can be improved only by early diagnosis, every effort should be made to achieve this goal. This ambition may be responsible for the incorrect positive diagnosis often made in cases in which the vascular changes were small and circumscribed. Carcinoma of the pancreas when small usually causes localized changes while the changes in inflammatory disease are more generalised, exceptions occur however as evident in the present material. Moreover the vessels, when encased by pancreatic carcinoma appear irregular while the involvement in pancreatitis usually causes more regular changes. Differentiation will usually be possible with these rules in mind but only great personal experience will be effective in exceptional cases.

This investigation was based on a retrospective assessment a method which necessarily implies many errors. Considering this, however it may be stated that selective visceral angiography properly applied is of great value in diagnosing carcinoma of the pancreas.

SUMMARY

The findings in 116 patients with verified carcinoma of the pancreas have been examined. A correct preoperative diagnosis had been made in 79 and a retrospective diagnosis was possible in an additional 30 patients. An incorrect positive diagnosis was made in 18 patients preoperatively and in 5 patients retrospectively, a common cause being localized pancreatitis. Variations in the vascular anatomy and a poor technique contributed to other errors in diagnosis.

ZUSAMMENFASSUNG

Die Befunde bei 116 Patienten mit einem nachgewiesenen Karzinom des Pankreas wurden untersucht. Eine richtige präoperative Diagnose wurde in 79 Fällen gestellt und eine retrospektive Diagnose war bei weiteren 30 Patienten möglich. Ein falsche positive Diagnose wurde bei 18 Patienten präoperativ und bei 5 Patienten retrospektiv gestellt. Eine gemeinsame Ursache war eine lokalisierte Pankreatitis. Abweichungen in der Gefäßanatomie und eine unzureichende Technik trugen zu anderen Fehlern in der Diagnose bei.

RÉSUMÉ

L'auteur a examiné les signes radiologiques de 116 malades atteints d'un cancer étiré du pancréas. Le diagnostic préopératoire correct a été fait dans 79 cas et un diagnostic retrospectif a été possible chez 30 autres malades. Un diagnostic faussement positif a été fait avant l'opération chez 18 malades et retrospectivement chez 5 malades, une cause fréquente de diagnostic faussement positif était une pancréatite localisée. Les variations de l'anatomie vasculaire et une mauvaise qualité technique ont contribué aux autres erreurs de diagnostic.

REFERENCES

- BRALL S M DYER G A and STEPHENSON H E Disappointments in the management of patients with malignancy of pancreas duodenum and common bile duct Arch Surg 101 (1970) 461
- BOUYEN E Angiography in pancreatic disease Acta gastro-ent belg 33 (1970) 391
- Pancreatic angiography I Angiography Second Edition Edited by H J Abrams Little Brown and Company Boston 1971
- and TYLER U Vascular changes in chronic pancreatitis Acta radiol Diagnosis 12 (1972) 34
- BOOKSTEIN J J REUTER S R and MARTEL W Angiographic evaluation of pancreatic carcinoma Radiology 93 (1969) 757
- BUCK B A and FLETCHER W S Carcinoma associated with pancreatic cyst Surg Gynec Obstet 134 (1972) 44
- BURAKIANI S and BOM S The significance of the celiac phase of celiac and superior mesenteric arteriography in evaluating pancreatic carcinoma Radiology 102 (1972) 11
- BOCHNER E BOLDT I FROMMELDT H und KAUFER C Die angiographische Diagnostik der Pankreastumoren und der Pancreatitis Fortschr Röntgenstr 115 (1971) 726
- CHILD C G and FLETCHER C F Pancreaticoduodenectomy Surg Clin N Amer 46 (1966) 1201
- FEDUSA N J DENT T L and LINDEBAUER S M Results of palliative operation for carcinoma of the pancreas Arch Surg 103 (1971) 330
- FREEDMAN M EDELMAN M and HOLST NIELSEN F The value of selective angiography in the diagnosis of tumours in pancreas and liver Radiology 93 (1969) 765
- GLENN F and THORBJARNARSON B Carcinoma of the pancreas Ann Surg 159 (1964) 945
- HERMANSER CL EGARLAT B et BERGUTH V L'artériographie des tumeurs pancréatiques J Radiol Électrol 48 (1967) 327
- KALDITRUP H E Carcinoma of the pancreas A statistical clinical and pathological study Acta his scand (1966) Suppl No 362
- KRAHN L S The rising incidence of carcinoma of the pancreas An epidemiological appraisal Amer J Gastroent 54 (1970) 500
- LECHNER G LÖWENBERG H ZATSEVICH W und BRUCKER P Zur angiographischen Diagnose des Pankreaskarzinoms Fortschr Röntgenstr 113 (1970) 540
- LEIDY H FAIRBLANDER H J und MAURER W Arteriographische Diagnostik von Karzinomen des Pankreasorgans und sekundäres Schwere med Wochr 96 (1966) 871
- LUNDENBERG A Angiography in carcinoma of the pancreas Acta radiol (1965) Suppl No 235
- MIRANEY T F and BLONKOWICZ E Arteriographic manifestations of pancreatic neoplasms Amer J Roentgenol 95 (1965) 770
- MILLER J R BACOMARUM A H and COMPTON M W Carcinoma of the pancreas effect of histological type and grade of malignancy on its behavior Cancer 4 (1951) 233
- NEWMAN R A and POLLARD J J A critical evaluation of selective celiac and superior mesenteric angiography in the diagnosis of pancreatic disease particularly malignant tumor facts and artefacts Radiology 89 (1967) 1017
- NORDAUM M BOM S KJELDSE H and BLANKENHORN W Selective mesenteric arteriography in the diagnosis of pancreatic lesions Amer J Gastroent 48 (1967) 121
- OLSSON O Angiography in tumours of the pancreas In Modern trends in diagnostic radiology Edited by J W McLaren Butterworths London 1970

- POPE N A and FISH J C Palliative surgery for carcinoma of the pancreas *Amer J Surg* 121 (1971) 271
- REUTER S R, REDMAN H C and JOSEPH R R Angiographic findings in pancreatic carcinoma *Amer J Roentgenol* 107 (1969) 56
- REUTER S R, REDMAN H C and ROOKSTEIN J J Differential problems in the diagnosis of carcinoma of the pancreas *Radiology* 96 (1970) 93
- ROUCH J and BRYT J Angiography of the pancreas *Amer J Roentgenol* 94 (1965) 187
- SAWYER B P, NEAL M P, ARMSTRONG R H and HAGER H D Ten years experience with coeliac and upper abdominal superior mesenteric arteriography *Amer J Roentgenol* 101 (1967) 345
- SUZUKI T, LAWRENCE K, NAKAYAMA A, TAKEDA H, KOBAYASHI K, KASUTO N and HORIO I Selective arteriography in cancer of the pancreas at a resectable stage *Amer J Surg* 122 (1971) 402
- TAVERNIER J, DELORME G, LAFITTE J, TILLYER J et BELLET M Apports d'angiographie coeliale et mésentérique à la radiographie pancréatique *J Radiol Électrol* 50 (1969) 867
- TYLÉN U Angiographic differentiation between inflammatory disease and carcinoma of the pancreas *Acta radiol Diagnostica* 14 (1973) 257
- and AURELIO B Angiographic diagnosis of inflammatory disease of the pancreas *Acta radiol Diagnostica* 14 (1973) 215
- WÄNGBLÖDER W, RADTKE U, NUDMAN H und EMMERICH J Pankreasdiagnostik durch selektive Angiographie *Röntgen Bl* 20 (1967) 501

OVARIAN VESSELS AND URETER AS INDICATORS OF THE EXPANSION OF THE UTERUS IN PREGNANCY

A roentgenographic and statistical investigation

LARS OHLSON

A method for statistical topographic recordings in the abdomen has already been presented (OHLSON 1972). This included a two-dimensional coordinate system based upon the constancy of certain skeletal reference points. The displacement of the ovarian artery in pregnancy was recorded in this system in order to test the usefulness of the method: the course of the artery changed with a distinct regularity and the displacements were significantly different on the right and left sides. A subsequent investigation was directed to the anatomy of the ovarian artery and vein as well as of the ureter in the non pregnant state correlated to the findings at dissection (OHLSON 1973). The asymmetric position of the aorta and the asymmetry of the para aortic structures were reflected in the course of the ovarian artery whereas the retroperitoneal space lateral to the para aortic division, including the ovarian vessels and the ureters, was symmetric. This also implied that in the non pregnant state the asymmetric anatomy of the abdominal organs was not reflected by the course of the ovarian vessels or ureters.

The present investigation was concerned with the primary expansion of the pregnant uterus as reflected by the course of the ovarian vessels and the ureters

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and by the displacements of abdominal structures caused by the expansion

Earlier investigations The oldest known anatomic representation of the ovarian vessels in a drawing from about 1510 of the uterus in late pregnancy by LEONARDO DA VINCI with the terminal parts of the vessels passing the ovary together on their way to uterine cornu. The vein is enlarged and almost straight while the artery much smaller pursues a winding course along its upper aspect. No description of the vessels appears however in the notes accompanying the drawings or in the other manuscripts preserved from LEONARDO'S anatomic investigations.

HUNTER (1774-1794) made detailed examinations of the pregnant uterus in a series of autopsy cases from the third month to term. This author also investigated the broad ligament and its contents *in situ* by injecting wax into the ovarian, uterine, and round ligament vessels. However, no possibility existed of examining the ovarian vessels *in situ* in the peritoneal fold of the uterus proximal to the ovary, nor was the course of the vessels in the posterior abdominal region described.

The first arteriographic demonstration of the ovarian artery in pregnancy was made by DOS SANTOS (1931) who obtained filling of the right artery in one case in the sixth month.

The transformations of the pregnant uterus were also described by HUNTER (1794) who stated "The uterus adapts itself to the neighbouring parts and to the attitude of the body and moulds itself into various shapes from accidental circumstances and further the projections of the spine and the psoas and iliac vessels mould the outside of the uterus into corresponding cavities."

The pressure on the posterior abdominal wall from the uterus was demonstrated by KERR et coll. (1964) by the presence in normal late pregnancy of obstruction to the flow in the inferior vena cava with the patient supine and which immediately ceased upon elevation of the uterus.

Several authors (NEUMANN 1933, STANDER 1941, KEHRER 1952) expressed the view that the position of the placenta exerts a determining influence upon the extent of hypertrophy of the uterus, the part to which it is attached enlarging more rapidly than elsewhere. The uterine ends of the round ligaments are thus supposed to be close together when the placenta is inserted upon the posterior wall and far apart when it lies on the anterior wall.

No reports of roentgenographic investigations of the ovarian vein in pregnancy appear to have been published.

In describing the dilatation of the ureters in pregnancy, several authors mention that the abdominal portion of the ureter is displaced laterally from the fourth month of pregnancy to term, occasionally reaching as far from the spine as 10 cm (BAIRD 1935, SCHUMACHER 1933, KEHRER 1952). The individual

variations appear to be great: the ureter was even found to be displaced medially (HEHRER)

Material The roentgenographic series was the same as that described in a previous report (OHLSON 1972). The cases were divided into periods related to the duration of pregnancy for the statistical analysis of mean values in the same way as in the report mentioned. Regression analysis was related to the duration of pregnancy in weeks.

The examinations at laparotomy in late pregnancy comprised 8 cases in which caesarian section was performed.

Methods

Roentgen investigations The positions of the structures were recorded in the topographic coordinate system presented in a previous report (OHLSON 1972). The course of the ovarian artery was thus defined by certain points dividing it into parts. The part of the artery running from its origin to point 0 was defined as the pre aortic part: this designation being used by virtue of the findings at dissection (OHLSON 1973). In the a p projection the accuracy of location of the origin was 2 to 3 mm: the level of the origin was defined as the longitudinal position of point 0 (y coordinate) and correlated to the longitudinal extent of the pre aortic part.

Complementary projections comprised oblique projections with the patient turned 45° to the right and left and a lateral projection. Measurements were made to an accuracy of 1 mm except for the above mentioned limitation in the determination of the origin in the a p projection, and for the width of the artery and distances between point 0 and the wall of the aorta which were measured to an accuracy of 0.5 mm.

The configuration of the ovarian artery was recorded with respect to its tortuosity. This was described by recording the distribution along the artery of three kinds of distinctive figures: curves, axials and loops (Figs 1 to 6).

The configurations of the anastomoses between the ovarian, uterine and round ligament arteries were examined.

The course of the ovarian vein was plotted by the normal (midline) of its contours in the a p plane and recorded in the topographic coordinate system. Two parts of the vein corresponding to parts 2 and 3 of the artery were determined. The statistical analysis of the vein was confined to the left side and to periods 4 to 7. The vein sometimes reached a maximum caudal point and from there turned cranially in the same way as the artery. This point was defined as the turning point of the vein. It could be analyzed statistically in periods 4 to 6.



Fig 1 Roentgenogram of characteristic course of the ovarian artery (\rightarrow) and ureter in a case in late pregnancy (33 weeks). Scale 1:3 (Cf. Ohlson 1972 Figs 6 and 7)

The position of the uterine wall was recorded in relation to points 3 and 4.

The site of the placenta was examined on the assumption that hypertrophy of the uterine wall at the placental site might change the position of the anastomosis: the site was therefore recorded with regard to its longitudinal position in relation to the anastomosis on each side. The positions were divided into placenta situated entirely above or below the anastomosis and into those lying mainly above or below the anastomosis but also extending beyond that point.

The course of the ureter was recorded in the same way as that of the ovarian vein.

The course of the superior mesenteric artery was related to the uterine wall. The number of cases was too small to permit statistical analysis in the coordinate system. The course of the inferior mesenteric artery was investigated in relation to the uterine wall and the ovarian vessels on the left side but not in the coordinate system because the number of non pregnant cases was too small for statistical analysis.

The examinations performed in the complementary projections were too few for statistical analysis. The course of the vessels in relation to other structures was correlated to that in the a-p plane.

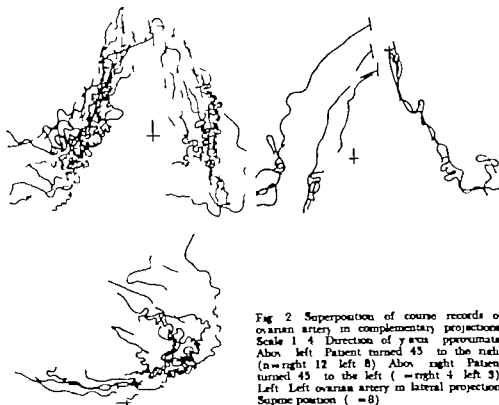


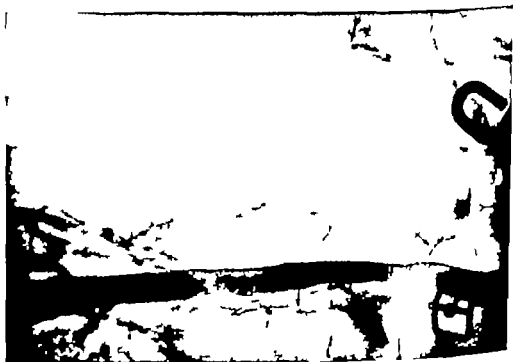
Fig. 2 Superposition of course records of ovarian artery in complementary projections. Scale 1:4. Direction of y-axis approximate. Above left: Patient turned 45° to the right (n=right 12 left 8). Above right: Patient turned 45° to the left (n=right 4 left 3). Below left: Left ovarian artery in lateral projection. Superposition (n=8).

Examinations at laparotomy in late pregnancy. The uterus and its peritoneum were examined by inspection and palpation. The uterus was not elevated. After delivery of the child, the relations of the uterus and its appendages to the abdominal and pelvic structures were examined. The uterus was anteverted and turned to each side for inspection and in certain cases for resection of the tubes.

Results

Roentgen examinations

The course of the ovarian artery. The characteristic course of the ovarian artery at arteriography in a case in late pregnancy appears in Fig. 1 and the displacements in pregnancy on each side are recorded in the coordinate system (see OHLSSON 1972 Fig. 3). The statistical data not given in the text appear in the Table and in previous reports (OHLSSON 1972, 1973). Figs 2 and 3 depict the



b

Fig. 3 Roentgenogram of characteristic course of ovarian artery (→) in late pregnancy in lateral projection. Top 33 weeks. Bottom 33 weeks. Turning point (→) anastomosis (→) inferior mesenteric artery (→).

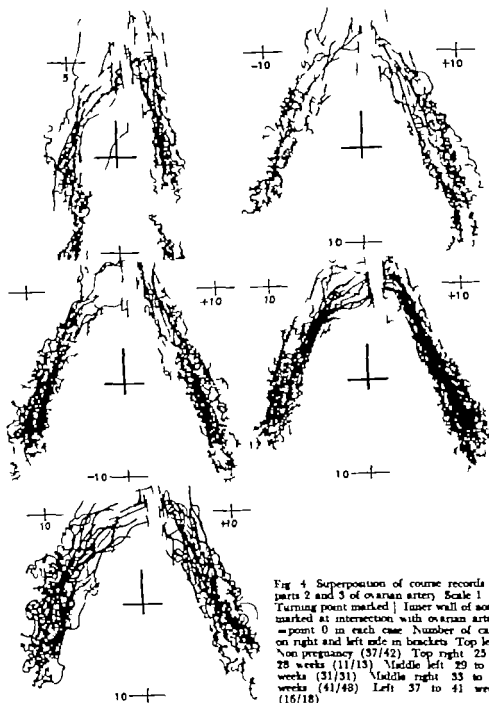


Fig 4 Superposition of course records of parts 2 and 3 of ovarian artery. Scale 1-4. Turning point marked | Inner wall of aorta marked at intersection with ovarian artery = point 0 in each case. Number of cases on right and left side in brackets. Top left Non pregnancy (37/42). Top right 25 to 28 weeks (11/13). Middle left 29 to 37 weeks (31/31). Middle right 33 to 36 weeks (41/48). Left 37 to 41 weeks (16/18).

Table

Directions of different parts of the ovarian artery. Part 2: Angle between y axis and the straight line connecting points 0 and 2. Part 2+part 3: Angle between y -axis and the straight line connecting points 0 and 3.

	Period								
	2			3			4		
	Mean	SD	n	Mean	SD	n	Mean	SD	
Part 2									
Right side	41	10	5	45	9	4	42	9	7
Left side	26	4	5	30	7	7	28	5	11
Part 2+part 3									
Right side	34	9	5	36	5	4	34	6	7
Left side	27	3	5	24	4	7	26	7	11

Linear regression analysis of decrease in angle between y axis and different parts of the ovarian artery in pregnancy. Part 1: Right side $p < 0.01$ left side $p > 0.05$. Part 2: Right side $p < 0.01$ left side $p > 0.05$. Part 2+part 3: Right side $p > 0.05$ left side $p < 0.05$.

course of the artery in the complementary oblique and lateral projections. The coordinate superposition of course records in the $a-p$ plane appears in Fig. 4.

The level of origin (y coordinate of point 0) in non pregnancy was $+8.8 \pm 1.8$ ($n=16$) on the right and $+9.4 \pm 2.0$ ($n=19$) on the left side and in pregnancy $+9.1 \pm 1.8$ ($n=55$) on the right and $+9.5 \pm 1.8$ ($n=79$) on the left side. There were no significant differences between the levels on the right and left sides, nor between the non pregnant and pregnant states.

The part of the artery proximal to the inner wall of the aorta (the pre aortic part) in the $a-p$ projection was evident on the right in 29 cases and on the left side in 8 cases. The right ovarian artery in this projection proved to arise from the anterior aspect of the aorta in 18 cases, since the pre aortic part was projected to the left of the origin of the corresponding right lumbar arteries. In the complementary oblique projections (Fig. 6) the pre aortic part was evident on the right in 4 cases and on the left side in 3 cases. The artery formed a small angle with the wall of the aorta. The artery was not found to arise from any other than the anterior aspect of the aorta.

The course and configuration of part 1 of the ovarian artery in the coordinate system in relation to the duration of pregnancy appears in Fig. 5. The configuration on the right side was almost straight or lightly tortuous: no curves, axials or loops were present. The angle to the y axis was $47 \pm 15^\circ$ in non pregnancy

Tabl (cont.)

5			6			7		
Mean	SD	n	Mean	SD	n	Mean	SD	n
48	9	11	50	10	9	57	4	6
29	5	15	51	5	10	50	9	8
37	5	11	38	10	9	40	3	6
25	4	15	28	6	10	29	5	8

($n=16$) and 67 ± 18 in pregnancy ($n=55$). The angle was larger in pregnancy than in non pregnancy ($p < 0.001$) and increased in relation to the duration of pregnancy ($p < 0.01$). The position of point 0 was to the left of the y axis (for the non pregnant cases $x = 0.4 \pm 0.5$ and for the pregnant cases 0.5 ± 0.6 mm).

The course of the artery in the complementary oblique projections was precal in case 5 (Fig. 6). The artery in this case also ran perpendicular to the film plane at its passage in front of the vein. In cases 6 and 7 the passage of the artery was so close to the spine as to be compatible with a retrocaval course.

The configuration of part 1 on the left side varied from almost straight to markedly tortuous. Point 0 was axial in 28 cases; distal to that point the artery was axial in 9 cases (Fig. 5), in 6 of which this course coincided with the lateral aspect of the psoas muscle. One curve was present in 19 cases, no loops were present. The angle was 38 ± 12 in non pregnant ($n=19$) and 41 ± 16 ($n=19$) in pregnant cases. There was no significant difference between these cases nor of change during pregnancy. Point 0 was situated 2.3 ± 5.2 mm to the right of the left contour of the spine, varying between 15 mm to the right and 10 mm to the left of the contour ($n=98$). In 54 cases, the artery took a cranial course from point 0 with an almost straight configuration for a distance varying from 1 to 25 mm, the average being 5.2 mm. In the remaining cases the artery

Fig. 5. Course and configuration of part 1 of right and left ovarian arteries in the coordinate system. Scale 1:4. Duration of pregnancy in weeks.

did not run cranial to point 0 (Fig. 5). The approximate angle immediately distal to point 0 varied between 0 and 200° the average being $114^\circ (\pm 50^\circ)$ ($n=98$). The artery in cases 1 and 2 passed from point 0 in a dorsal, lateral and cranial direction and then turned caudad in the complementary oblique projections (Fig. 6). Part 1 appeared in the lateral projection in 1 case running from point 0 in a cranial and dorsal direction and then caudally.

Part 1 on the right side thus crossed the vertebral column, gradually diverging in relation to the duration of pregnancy, whereas on the left side it lay to the left of the spine and retained this position and course throughout pregnancy.

Distal to part 1 the artery took the same course in early pregnancy (period 1) as in non pregnancy (period 0) passing in a caudal direction in front of the psoas muscle and entering the pelvis in front of the iliac arteries. It turned medially to the anastomosis near the tubal end of the ovary. In these periods the turning point, ovary and anastomosis were situated in the pelvis without any significant asymmetry between the sides.

From period 1 to period 2, the turning point, ovary and anastomosis passed into the abdomen to a position close to the lateral aspect of the psoas muscle. From period 2 onward the right turning point was stationary and more cranial than the left ($p < 0.001$) while the left turning point passed for a short distance in a cranial and lateral direction ($p < 0.01$). The ovaries were consistently situated at or a little above the turning points (no significant difference in location of the ovary and the turning point). The anastomosis was displaced more than the other point and more on the right than on the left side. It passed the turning point and the ovary in period 2 and then approached point 2. At term it was bilaterally almost as cranial as this point but more lateral. From period 2 onwards, part 4 accordingly took an increasingly cranial course.

On the right side part 2 gradually diverged ($p < 0.01$) to form an arch over the quadratus muscle while the divergence of part 3 diminished accordingly. On the left side part 2 diverged up to period 2 but not later ($p > 0.05$). Thus, on the left side both part 2 and part 3 remained close to the lateral aspect of the psoas muscle.



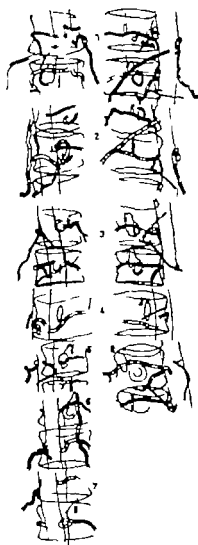


Fig. 6 Part 1 of ovarian artery in complementary oblique projections. Scale 1:4. Cases 1 to 4 patient turned 45° to the right and left cases 5 to 7 to the right only and case 8 to the left only. Duration of pregnancy: case 1 40 weeks case 2 40 weeks case 3 32 weeks case 4 not pregnant case 5 29 weeks case 6 36 weeks case 7 38 weeks and case 8 23 weeks.

The configuration of the ovarian artery (Figs 1 to 6) Part 2 was almost straight or slightly tortuous. Near point 2, the tortuosity increased, part 3 being consistently more tortuous than part 2 in the individual case. The tortuosity varied from one case to another as well as from side to side. Thus part 3 was less tortuous in certain cases than part 2 in other cases. Part 4 generally passed in a curve cranial to the anastomosis into which it thus entered in a caudal direction (Fig. 3).

The axial length and the straight length of parts 2 and 3 were proportional in all periods. The straight length of part 4 decreased from non pregnancy to period 2 but then increased constantly, exceeding that of non pregnancy from period 3. The axial length of part 4 did not change, the tortuosity of that part being merely proportional to its straight length.

Branches from parts 2 and 3 appeared in 3 cases on the right and in 5 cases on the left side. They were small (transverse sectional area 0.2 to 0.8 mm²) and their terminations could not be demonstrated. Branches from part 4 generally filled; they were small. No change in the width of the artery distal to the site of branching was evident.

The anastomoses of the ovarian artery with the uterine and round ligament arteries had a characteristic configuration occurring at approximately right angles (Fig. 3). Part 4 was bifurcated on the right side in 2 cases and on the left side in 2 cases, forming a double anastomosis with the uterine artery. The round ligament artery anastomosed directly with the right ovarian artery in 2 cases. These variations appeared not to affect the position of the ovarian artery.

The course of the ovarian vein and the ureter as analyzed in the coordinate

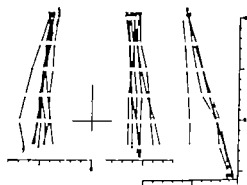


Fig 7 Course of left ovarian vein (right) and ureters (left) in the topographic coordinate system. Scale 1:4. Periods of pregnancy indicated by numbers.

system is presented in Fig 7 and analyzed by coordinate superposition appears in Figs 8 to 10.

The course of the left ovarian vein followed that of the artery. The turning point of the vein coincided with that of the artery (ovarian artery $x = +10.9 \pm 1.5$, $y = -6.9 \pm 2.1$ ($n = 26$); ovarian vein $+10.2 \pm 1.3$, -7.3 ± 2.1 ($n = 15$)).

The pampiniform plexus was not found to extend into part 3.

No correlation between the width of the vein and that of the artery was evident ($r = 0.042$).

The position of the uterine wall. In periods 0 and 1 the turning point was lateral to the uterus behind which no part of the artery passed. From period 2 onwards the uterus covered the artery to an increasing extent. The uterine wall on the right side gradually moved lateral to the turning point ($p < 0.001$), whereas on the left side it coincided with the point (no significance for difference in position). The uterus was dextroverted ($p < 0.001$).

The placenta was situated entirely above the anastomosis on the right side in 40 per cent and on the left side in 37 per cent of cases; it lay below the anastomosis on the right side in 12 per cent and on the left side in the remaining 11 per cent of cases ($n = 87$). The proportions of placentas reaching beyond the anastomosis were 23, 23, 23 and 20 per cent, respectively. There was thus no significant asymmetry of the site of the placenta.

The ovary was evident more often on the left than on the right side. Its form and size appeared not to affect the course of the ovarian artery or vein. (A corpus luteum is depicted in Fig 11.)

The ureter remained in its non-pregnant position at levels $+10.0$ to $+5.0$ (Fig 7). From level $+2.5$ to level -2.5 it was displaced laterally from non-

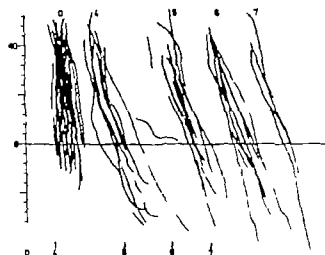


Fig 8 Superposed course records of left ovarian vein. Scale 1:4. Periods of pregnancy indicated by numbers and y axis by vertical bars.

pregnancy to pregnancy ($p < 0.001$) and continued to move throughout pregnancy (Figs 8-11 Table) ($p < 0.001$). The displacement increased in a caudal direction, reaching its maximum between levels 0.0 and -2.5 i.e. just above the iliac artery. There was no significance for asymmetry. Unlike the ovarian vessels, the ureter sometimes maintained its non-pregnant course (increase in standard deviations for levels +2.5 to -2.5 $p < 0.01$). The displacement of the ureter was thus significantly different from that of the ovarian vessels ($p < 0.001$).

The superior mesenteric artery was displaced cranially passing behind the uterus to the intestines.

The inferior mesenteric artery. Its origin moved to the left with the displacement of the aorta during pregnancy. Its main trunk and the superior part of the superior rectal artery also moved to the left. The branches of the sigmoid artery generally passed immediately above the ovarian vessels being displaced cranially

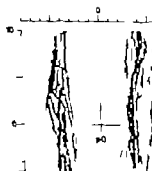


Fig 9 Superposed course records of ureter. Scale 1:4. Non-pregnant state. (Cf Fig 10).

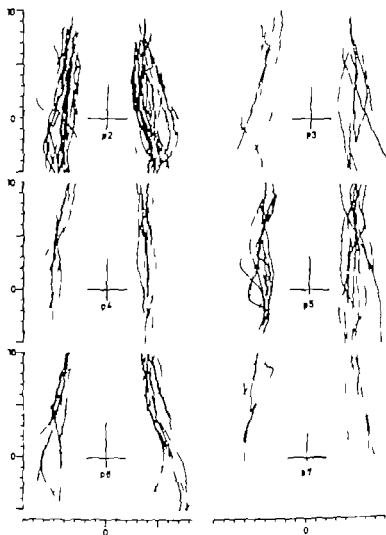


Fig 10 Superposed course records of uterus Scale 1-4 p~period of pregnancy (Cf Fig 9)

at the turning point and lateral to that point assuming a markedly caudal course

Other roentgenographic features not apparently indicative of the dynamics of pregnancy are described in other reports

Examinations at laparotomy in late pregnancy

In one case, the broad ligament and its proximal continuation were seen as far as the turning point on the left side extending over the anterior and lateral



Fig. 11 Corpus luteum of pregnancy 19 weeks

convexity of the uterus two venous trunks of irregular shape and an approximate diameter of 1 to 1.5 cm were present. The artery followed the upper aspect of the vein and entered the uterus above the vein. Proximal to the ovary the vessels were markedly mobile in relation to the peritoneum; the mobility decreased towards the uterus but was still much greater than that in the broad ligament in the non-pregnant state. The tube was attached about 3 cm above the anastomosis; it was almost straight, and passed in a caudal and posterior direction to the tubal end of the ovary. The round ligament was attached at the same level as the anastomosis and about 3 cm anteriorly. It extended over the corpus uteri and could easily be elevated in a fold. The colon bulged over the peritoneal fold at the turning point. Proximal to this point the vessels could be palpated in the edge of the fold as a loose cord running between the uterus and the lateral abdominal wall to the posterior abdominal wall.

One of the uterine cornua and the peritoneal duplicature corresponding to the ovarian ligament could be inspected in the other cases. The continuation of the fold could be palpated as in the case described. The findings were the same as in that case except for marked individual variations in the calibre of the ovarian vein.

After delivery of the child and removal of the placenta the cornua were still level with the pelvic inlet or slightly above it. The medial part of the lateral (anterior) layer still covered the anterior surface of the corpus uteri continuing into the parametrial peritoneum without demarcation. On antelexion of the



Fig. 12 Displacement of branches of inferior mesenteric artery (\rightarrow) by ovarian artery (\rightarrow)

uterus the peritoneal fold on both sides was stretched. The ovarian vessel passed in the edge of the fold over the psoas muscle and across the pelvis to the cornua. The peritoneum and the vessels moved freely in relation to one another and to the underlying structures. When the uterus was turned to one side, the duplicature on that side slackened and thereby disappeared while on the other side it became still more stretched. The posterior peritoneal layer continued without demarcation into the peritoneum coating the uterus, and with it into the recto-uterine pouch. The pouch was still narrowed by the enlarged uterus, but its floor was preserved. This retro uterine cavity thus formed a narrow space as deep as the length of the uterus and the height of the posterior peritoneal layer on each side.

Discussion

The ovarian artery proved to be mobile along its entire course at laparotomy and on anatomic dissection. Beneath the level parietal peritoneum of the posterior abdominal wall it could thus easily be elevated into peritoneal folds. In the extension of the retroperitoneal space forming the broad ligament it was mobile with the edge of the duplicature and with the exception of the part adjacent to

the mesovarium also within the duplicature. The artery may thus be likened to a cord suspended between its points of attachment at the aorta and the uterus capable of reflecting forces applied to the parietal peritoneum, whether level or duplicated. The ovarian vein after meeting the artery had the same course and mobility as the latter. The mobility of the vessels was much greater immediately after delivery than in non pregnant cases. The ureter completing the number of structures in the retroperitoneal space lateral to the para aortic division possessed a mobility similar to that of the vessels.

In non pregnant cases the retroperitoneal space was asymmetric in its para aortic division (aorta, vena cava and prevertebral structures) but not lateral to it. Furthermore the ovarian artery ran an asymmetric course in the para aortic division although not lateral to it. The abdominal topographic relationships of the retroperitoneal space, in contrast, were asymmetric both in front of and lateral to the para aortic division. Thus on the right side the root of the mesentery and the ascending mesocolon could be readily loosened from the peritoneum by turning the small intestine outwards and upwards while on the left side the fatty descending mesocolon was fused to the peritoneum (except for the intersigmoid recess) and permanently attached by its continuity with the rectum. Further the ligament between the caecum and the peritoneum was attached above the pelvic inlet while that of the sigmoid colon adapted to the oblique lateral border of the recess was attached at the inlet and more laterally.

The asymmetry of the abdominal organs in non pregnancy was thus not reflected in any asymmetry of the ovarian artery. This is in agreement with the course of the artery under the peritoneum of the posterior abdominal wall and with the absence of any constant asymmetry of the broad ligaments. The ovarian artery under non pregnant conditions thus proved to be an indicator of the state of symmetry of the retroperitoneal space, but not of the state of symmetry of organs invested in peritoneal duplicatures. These conditions determine to some extent the mode of transformation of the abdominal region in pregnancy.

The spatial effects of the primary changes in the ovaries and tubes in pregnancy are apparently negligible in proportion to the expansion of the uterus. (It was apparent that the elongation of the tubes is not a primary factor but secondary to the growth of the uterus.) The uterus may thus be regarded as the only constant primary expanding factor in pregnancy.

The expansion of the uterus produces pressure and traction. These two forces are sometimes combined whereas in other instances the anatomic conditions are compatible with the presence of only one of them. The pressure is well documented in the literature. HUVERA (1794) described the alterations in shape of the abdomen with postural changes and inferred the presence of reciprocal alterations in pressure and shape between the uterus and the surrounding structures.

The pressure on the posterior abdominal wall was demonstrated by KERR et coll (1964). In late pregnancy and in the supine position, displacement and compression of the aorta, the right common iliac artery, and the lumbar arteries also occur (OHLSON in preparation). The alteration in shape and consistency of the abdomen during uterine contraction is one of the signs of redistribution of pressure.

The traction exerted by the growing uterus is barely considered in the literature. STANDER (1941) stated: in pregnancy considerable tension is exerted upon the broad ligaments which then become unfolded at their median and lower portions and thus contribute to the mobility of the pelvic peritoneum which is characteristic of pregnancy. No other references have been found. The traction extends from the uterus into its peritoneal duplicatures, which in turn exert traction upon the abdominal structures that come in contact with them. Two of the structures of the retroperitoneal space in the non pregnant state, the ovarian artery and vein, form an integral part of the posterior abdominal wall as well as of the uterus and its peritoneal folds and consequently the asymmetric pattern of displacement of the vessels in the coordinate system reflects some of the effects of the asymmetric anatomy of the abdominal region. Since the third structure of the space, the ureter, is not attached to the uterus, it indicates some of the reactions to the expansion of the uterus of those parts of the space that remain close to the posterior abdominal wall.

The turning point is bound to transmit upward traction from the anastomosis into downward traction in the proximal parts of the artery.

The conditions described lead to the following conclusions regarding the mechanisms involved in the process of the growing uterus. The uterine cornua pull the edges of its peritoneal folds containing the ovarian artery and vein into the abdomen and at the same time the ligament is pushed to the side by the uterus. The original broad ligament disappears and is replaced by a fold that migrates in the course of the pregnancy along the abdominal wall, from which it extends in a large crescent around the uterus. When its edge meets the insertion of the mesentery and the sigmoid colon it pulls these structures with it but is also held back by them. The anterior layer is deflected so that the vesico uterine pouch disappears while the posterior layer remains attached to the lower uterine segment creating a deep, narrow space behind the uterus. The uterus presses against the posterior abdominal wall, pushing the arteries aside and the right artery upwards as well, while the left artery remains in the groove between the psoas and quadratus muscles protected by the mesocolon. The ovarian vein follows the artery. The ureter does not enter a peritoneal fold but is pushed aside by the uterus in the lumbar region. The conclusions will be discussed with reference to analogous parts of the ovarian artery on each side.

Part 1 The anisotropism of the origin of both ovarian arteries and the asymmetry of their course and configuration in non pregnancy are all expressions of the asymmetry of the para aortic division (For the retroperitoneal space and the artery alike this was the only region where asymmetry was present in the non pregnant state.) Much evidence accrued of pressure from the posterior wall of the uterus working in a cranial direction but with no possibility for constant traction in this direction. Thus the only possible cause of the increasing divergence of part 1 on the right side is pressure from the uterus. As the artery on this side runs in a space much narrower than on the left side even in the non pregnant state and which is moreover almost incapable of adapting to pressure the displacement can only result from compression by the uterus. Thus asymmetry also explains why on the left side the artery did not move, namely by its location to the side of the spine in front of the muscles, its involvement in fatty tissue and the interposition of the mesocolon between the artery and the uterus. If the traction reaches the origin of the artery the fixation of the origin imparts an equivalent countertraction. If it reaches part 1 it counteracts the effect of the cranial pressure on part 1 on the right side, and may also counterbalance an equivalent potential pressure on the left side.

The asymmetry of part 1 was thus an indicator of the pressure from the posterior wall of the uterus applied to the asymmetry of the region. The degree of actual displacement on the right and potential displacement on the left side could be counteracted by extension of the primary traction in the fold.

Part 2 The pressure of the uterus on the retroperitoneal space (which was symmetric in this region) is equivalent to that of part 1. The asymmetry of the artery increasing in pregnancy is consistent with the pre existing asymmetry of the abdominal region. The divergence on the right side was additionally enhanced by that of part 1 while no corresponding factor was present on the left side. Since the small intestine is displaced upwards by the expanding uterus the root of the mesentery and its continuation in the right mesocolon may become detached from the parietal peritoneum the anatomic conditions allow such a dissection. Provided this occurs the pressure from the posterior wall of the uterus will be additionally accentuated on the right while no analogous mechanism is possible on the left side. The cranial displacement of the trunk of the superior mesenteric artery and the ileal branches observed in this investigation suggested the presence of such a dissection but the number of cases was too small to prove it. It would be possible to investigate this problem by oral administration of contrast medium before radiologic examination in late pregnancy.

The asymmetry of part 2 thus reflected the asymmetry of the abdominal organs acting upon the symmetric retroperitoneal space.



Fig. 15 Course of left ovarian artery (\rightarrow) in relation to the colon and mesocolon. Inferior mesenteric artery (\dashrightarrow) a) 32 weeks b) 35 weeks c) 38 weeks

Part 3 The lateral movement of the cranial part on the right side was a function of the lateral and cranial movement of part 2 caused by the pressure from the posterior uterine wall and the smaller movement on the left side a function of the lower pressure exerted on both part 2 and part 3 on this side.

The asymmetry of part 3 thus reflected that of the abdominal organs acting upon the symmetric retroperitoneal space: the movements of parts 2 and 3 were therefore analogous.

Part 4 The right turning point in period 2 was located more cranial and lateral than the left point remaining in this position till term while the left turning point moved in a cranial and lateral direction to reach the position symmetric to that of the right point at term. The distance to the anastomosis from the turning point was the same on both sides and augmented symmetrically but the angle representing the direction of the primary traction was more lateral on the right side.

Since there was no asymmetry in the distribution of the placental site, the position of the anastomosis could be governed only by the asymmetry of the abdominal organs. The fixed location of the right turning point thus corre-



Fig 14 Lower border of anterolateral peritoneal layer on the right side delineated by contrast medium

sponded to the topography of the caecum and its connections with the parietal peritoneum, whereas the displacement of the left turning point corresponded to the topography of the sigmoid colon and its connections with the parietal peritoneum, i.e. the shape of the intersigmoid recess. The asymmetry of the turning points and the anastomoses thus reflected the effects of the asymmetric abdominal organs upon the symmetric retroperitoneal space causing asymmetry of the uterus and its peritoneal folds.

Roentgenography disclosed that the space between the uterus and the uterine peritoneal fold on the one hand and the lateral abdominal wall on the other was often occupied by the colon (Fig 13). The left colon was also invariably revealed by the inferior mesenteric artery (Fig 13) and in one case the space was filled at peritoneography (Fig 14). Laparotomy in late pregnancy indicated that the lateral layer was more extensive in all directions than the corresponding anterior layer of the broad ligament in the non pregnant state. These conditions permitted the extent of that layer to be determined. The lateral cranial and anterior displacement of the ovarian vessels in relation to the convexity of the uterus involving separation of them from the posterior abdominal wall was evident in the a.p. as well as the lateral and oblique projections (Figs 2 3 4). In late pregnancy the vessels passed 6 to 7 cm lateral and cranial to the insertion

at the pelvic inlet of the suspensory ligament of the ovary in the non pregnant state as well as anterior to that site. The edge of the fold thus arises in the posterior abdominal wall lateral to the psoas muscle and extends around the uterus following the shape of the narrow curved space formed by the uterus and the abdominal wall. Its relationship to the colon is asymmetric: on the right side the ovarian vessels pass between the uterus and the caecum, whereas on the left side they surround the part of the sigmoid colon that forms the medial border of the intersigmoid recess.

The uterine peritoneal fold of pregnancy differs so widely from the broad ligament in the non pregnant state that it might be expected to be composed more or less extensively of other structures. It could be inferred that at three sites it retains homology with the broad ligament, viz at the hilum of the ovary, at the passage into the uterine wall of the tube, ovarian artery and round ligament artery, and at the communication of the round ligament artery with the external iliac artery. The extension of the anterior layer over this area and its transgression onto the surface of the uterus, as evident in the present investigation, agree with the findings of HUNTER (1774).

The shape of the fold proximal to the ovary is dependent on the continuity of the lateral (anterior) and medial (posterior) layers. With the movement of the ovarian vessels, the marginal part of the lateral layer becomes gradually converted into that of the medial layer. The extension of the fold into the abdomen thus involves the transformation of the previously level peritoneum of the abdominal wall into a new mobile fold in which the ovarian vessels become increasingly separated from the posterior abdominal wall, without affecting the ureter. The elasticity of the peritoneum renders the area of realigned peritoneum smaller than that traversed by the vessels. Both the lateral and medial layers pass onto the uterus without demarcation, being widely separated from one another by the expansion of the corpus uteri into the parametrial tissue. Both layers reach their maximum height at the uterine cornu. The lateral layer indicated by the round ligament extends from the cornu to the inguinal ligament for a distance of about 15 cm. The medial layer extends from the cornu to the bottom of the retro-uterine pouch for a distance of about 20 cm.

The normal topographic relationships of these structures appear so far to have been accessible to a systematic investigation only by means of arteriography. The peritoneography performed in one single case indicates that this method is suitable for demonstrating the shape of the peritoneal folds. Oral ingestion of contrast medium would give further information about the displacement of the small intestine and of the colon on each side. Combined with angiography of the superior mesenteric artery, these methods would also indicate whether the root of the mesentery and the corresponding part of the ascending mesocolon are

loosened from the parietal peritoneum by the pressure from the uterus

HUNTER (1774-1794) investigated the uterine peritoneal fold at autopsy. However, in all cases but one, he resected it at the level of the ovary, thus being deprived of the possibility of examining the topographic relationships. In the remaining case, he turned down the empty uterus over the pubic bones. This case was apparently stored and examined in cold conditions. This seems to explain why the intestines, after removal of the pressure from the uterus, still revealed signs of that pressure—a phenomenon that would not be reproduced *intra vitam*. The ovarian vessels were also depicted to emerge from behind the caecum and the lateral border of the intercaecal recess and then extend over the external iliac vessels above the inlet to the empty uterus; they are not elevated in a fold. These conditions explain the differences between HUNTER's description and the results of the present investigation. These latter also explain certain contradictions between HUNTER's description and his plates. The statement that the spermatic vessels pass over the iliacs immediately to the side of the uterus contains a contradiction, for these vessels cannot pass to the side of the uterus unless separated from the iliac vessels. This could be inferred, but was also a consistent finding in the present investigation. The absence of a fold in HUNTER's case is explained by the previous emptying of the uterus. Had the organ been filled anew, the fold would have been restored. HUNTER's statement, "the broad ligament disappears, no more of it remaining than its upper and outer corner," appears somewhat vague for it is contradicted by his own illustrations of resected pregnant uteri; these demonstrate the above-mentioned preservation of the triangular area of the anterior layer. HUNTER designated the origin of the fold at the iliacs as the upper and outer corner. However, as evident in the coordinate system, the actual upper and outer corner is the one attached to the uterus; the anastomosis, both this corner and the upper and outer corner, as described by HUNTER, are preserved.

Acknowledgement

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SUMMARY

The changes in the course of the ovarian vessels and the ureter in pregnancy were analyzed in the topographic coordinate system described earlier and related to surrounding structures. The vessels reflected both the pressure and traction from the uterus, whereas the ureter reflected only the pressure on the posterior abdominal wall. The vessels were elevated into peritoneal duplicatures which developed in pregnancy, extending from the posterior abdominal wall around the uterus to its cornu.

ZUSAMMENFASSUNG

Die Veränderungen im Verlauf der Ovarialgefäße und dem Ureter während der Gravidität wurden in dem früher beschriebenen topographischen Koordinatensystem analysiert und zu den umgebenden Strukturen in Beziehung gestellt. Die Gefäße waren sowohl von Druck als auch vom Zug des Uterus abhängig, während der Ureter nur vom Druck auf die hintere Bauchwand abhing. Die Gefäße werden in einer peritonealen Duplikatur aufgehoben, die sich während der Gravidität entwickelt und sich von der hinteren Bauchwand um den Uterus zur Cornu uteri erstreckt.

RÉSUMÉ

L'auteur a étudié les modifications du trajet des vaisseaux ovaires et de l'uretère au cours de la grossesse en utilisant le système topographique de coordonnées décrit dans un travail précédent. Ces modifications ont été reliées aux structures voisines. Les vaisseaux subissent à la fois la pression et la traction de l'utérus alors que l'uretère ne subit que la pression sur la paroi abdominale postérieure. Les vaisseaux sont soulevés dans une duplication péritonéale qui se développe au cours de la grossesse et qui s'étend de la paroi abdominale postérieure autour de l'utérus jusqu'à ses cornes.

REFERENCES

- BAIRD D. The upper urinary tract in pregnancy and puerperium with special reference to pyelitis of pregnancy. *J. Obstet. Gynaec. Brit. Emp.* 42 (1935) 516.
- HUNTER W. The anatomy of the human gravid uterus. London 1774.
- An anatomical description of the human gravid uterus. London 1794.
- KAMMERER E. Anatomie und Physiologie der Schwangerschaft. In: *Biologie und Pathologie des Weibes*. Band VII, p. 299. Verlag Urban & Schwarzenberg, Berlin 1957.
- KERR M. G., SCOTT D. B. and SAMUEL E. Studies of the inferior vena cava in late pregnancy. *Brit. med. J.* 1964, 1, p. 532.
- LEONARDO DA VINCI. *Quaderni d'anatomia*. I e III. (In Italian.) Edited by O. Vangersten, A. Fonahn and H. Hopstock. Jacob Dybwad, Oslo 1911 and 1913.
- NEUMANN H. O. Krankheiten der Uteruswand einschließlich Beckenbodenewebe. In: *Handbuch der speziellen Pathologie, Anatomie und Histologie*. Band VII, Teil 2, p. 453. Herausgegeben von F. Hencke und O. Lubarsch. Springer Verlag, Berlin 1933.
- OHLSOHN L. Coordinated topographic recordings in the abdomen. The ovarian artery as an indicator of the expansion of the uterus in pregnancy. *Acta radiol. Diagnostica* 12 (1972) 705.
- Non pregnant anatomy of the posterior abdominal wall as reflected in the course of the ovarian vessels and ureter. A roentgenographic, statistical and anatomic investigation. *Acta radiol. Diagnostica* 14 (1973) 145.
- DES SARTRES R. *Arteriographie des membres et de l'aorte abdominale*. Masson & Co. Paris 1931.
- SCHUMACHER P. Die Röntgendiagnostik in der Geburtshilfe. In: *Ergebnisse der medizinischen Strahlenforschung*. Band IV, p. 235. Georg Thieme Verlag, Leipzig 1933.
- STANDER H. *Williams Obstetrics*. Eighth edition. D. Appleton Century Company Inc. New York 1941.

ANGIOGRAPHIC LOCALISATION OF A PHEOCHROMOCYTOMA IN THE ORGAN OF ZUCKERKANDL

Report of a case

Z. CZEJALA

Progress made in recent years in the diagnosis of the causes of hypertension has probably resulted in the more frequent detection of pheochromocytomas. Tumours of chromaffin tissue have sometimes been encountered in patients undergoing nephroangiography for hypertension or for possible renal malignancy. A patient with a pheochromocytoma with an unusual site and not indicated clinically is reported in this short paper.

Case report

Female, aged 43, admitted with polydipsia and polyuria (9 l/24 h) with headache and slight left epigastric pain together with hypertension and disturbance of vision for 15 years. Probable diabetes mellitus. BP 180/110. Urine sg 1004. ECG: ischaemia of the left ventricle. Nephroangiography: both kidneys and the suprarenal areas are normal. A richly vascularized tumour with well defined contours lay to the left of L2 to L4. The pathologic vessels were tortuous with irregular walls and pools of contrast medium were evident (Fig. 1). Selective angiography of the superior and inferior mesenteric arteries

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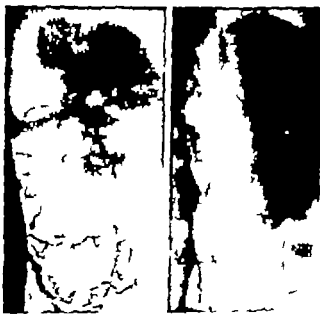


Fig 1 Nephroangiography a) Arterial phase Large richly vascularized tumour below the left renal artery close to the aorta b) Venous phase The contours of the tumour are well defined



Fig 2 Selective inferior mesenteric angiography a) The lower two-thirds of the tumour receive their blood supply from branches of the inferior mesenteric artery b) Venous phase

indicated that the lower two thirds of the tumour received its blood supply from branches of the inferior mesenteric artery (Fig 2) and the upper one third from branches of the middle colic artery. The type of vascularisation suggested a pheochromocytoma.

Operation revealed a mass in the retroperitoneal space just above the bifurcation of the aorta. The mass was removed.

Histology confirmed the diagnosis of pheochromocytoma. Blood pressure at 150/90 and unchanged a year later with the urine at 21/24 h.

DISCUSSION

The diagnosis of pheochromocytoma depends on the history, clinical signs, level of catecholamines, and localisation of the tumour (9-16) and may present difficulties (15). An additional difficulty may lie in deciding on the treatment as pheochromocytomas may occur wherever there is chromaffin tissue as many as ten per cent are localised in the extraadrenal area (2, 3, 4, 5, 6, 7, 10, 11, 12, 13, 14).

The pheochromocytoma now reported was unusual not only because of its uncommon site, the organ of Zuckerkandl, but on account of the presenting signs, particularly the polyuria of 9 l/24 h. The slight epigastric pain did not trouble the patient. The site of the growth was rare. MALTER & KOEHLER (1970) state that only 24 such cases have been reported and of these only three was diagnosed by angiography before operation.

Typical fluctuations in blood pressure did not occur (ALFORD *et coll.* 1969). Wide tortuous vessels and pools of contrast medium were evident as in other cases of pheochromocytoma and the tumour well defined.

Growths of this type of vascularity in the extraadrenal region should always suggest pheochromocytomas so that the plan of operation may be decided in advance.

SUMMARY

The angiographic and clinical features of an unusual case of pheochromocytoma arising from the organ of Zuckerkandl and localised by aortography and selective angiography of the superior and inferior mesenteric arteries are described.

ZUSAMMENFASSUNG

Die angiographischen und klinischen Merkmale eines ungewöhnlichen Falls mit einem Pheochromocytom ausgehend vom Zuckerkandlschen Organ und durch Aortographie und selektive Angiographie der Arteria mesenterica superior und inferior lokalisiert werden beschrieben.

RÉSUMÉ

L'auteur décrit les caractères angiographiques et cliniques d'un cas inhabituel de pheochromocytome provenant de l'organe de Zuckerkandl et localisé par aortographie et par angiographie sélective des artères mésentériques supérieure et inférieure.

REFERENCES

1. ALFORD R. J., GILL W. M. J. and KILL H. J. Angiography of adrenal neoplasms. *Amer. J. Roentgenol.* 106 (1966) 3.
2. BOGUSKI A., CIECHANOWSKI A., GUMA C. and POLSKA AKADEMIA UMIEJETOŚCI. Kraków 1972.

- 3 BOJTEK E, WILLIAMS C M and JUDKINS M P. Angiography of pheochromocytoma. *Amer J Roentgenol* 98 (1966) 225.
- 4 KAJAR P C and NICKERSON L V. Selective angiography of the adrenal glands. *Amer J Roentgenol* 101 (1967) 739.
- 5 KOHLER R and HOLST L R. Angiographic localization of suprarenal tumours. *Acta radiol. Diagnosis* 4 (1966) 21.
- 6 LAGERLÖF C. Angiographic changes in the adrenal glands. *Amer J Roentgenol* 101 (1967) 732.
- 7 LANTIER L O and ROSENCRANTZ M. Arteriographic appearance of pheochromocytoma. *Acta radiol. Diagnosis* 10 (1970) 35.
- 8 MALTER I J and KOEHLER P R. Angiographic findings in pheochromocytoma of the organ of Zuckerkandl. *Radiology* 97 (1970) 57.
- 9 MEANEY T F and BUONOCORE E. Selective arteriography as localizing and provocative test in the diagnosis of pheochromocytoma. *Radiology* 87 (1966) 309.
- 10 MÜNSTER W, WIERNY L and FORSTMANN W. Angiographie der Nebennierentumoren. *Fortschr. Röntgenstr.* 104 (1966) 367.
- 11 FORSTMANN W, WIERNY L and MÜNSTER W. Die selektive Nebennierenangiographie. *Fortschr. Röntgenstr.* 104 (1966) 150.
- 12 ROSE P. Arteriography in adrenal tumours. *Brit J Radiol* 41 (1968) 91.
- 13 —, KAUFMAN L, RUTENKA F F JR and PAXER W. Angiographic localization of pheochromocytoma. *Radiology* 86 (1966) 266.
- 14 SINGER K, CZEKAŁA Z, CZOPK J, LACIAK M, MARTELLO J, SŁOCH/ B i ZIMHARJ. Obecne poglądy na rozpoznawanie i leczenie guzów nadnerz. *Pol. Przegl. chir.* 43 (1971) 1601.
- 15 STURM A JR, SCHERJA H W and PUGETTES F. Differentialdiagnose der erhöhten Katecholaminausscheidung bei arteriellen Hypertonien. *Dtsch. med. Wochr.* 95 (1970) 826.
- 16 WERNIG G and SIEGENTHALER W. Diagnostik des Pheochromocytoms. *Dtsch. med. Wochr.* 96 (1971) 121.

Book reviews

ENDOSCOPIC COLOR ATLAS OF GASTRIC DISEASES By S. Ashizawa and T. Kodokoro 223 pages with 1884 mostly colored illustrations. Georg Thieme Verlag Stuttgart 1971. Price DM 178.

Gastroscopy and gastrophotography require much experience on the part of the examiner one that in the past could be acquired only by the carrying out of a large number of examinations with the inevitable mental mistakes. The introduction of improved instruments in recent years has greatly facilitated endoscopic examinations of the stomach the bulk of which can now be inspected. Photography with a gastrocamera achieves documentation of the endoscopic findings and pathologic changes may be assessed objectively. The authors of this book present 322 cases with a few gastrophotographs each being accompanied by an excellent sketch of the more important details. A photograph of the resected stomach is also often included although subtle changes are sometimes hard to distinguish without enlargement. As the circulation and tones are absent the photographs do little to augment the gastrophotographs and it may be that a representative roentgenogram of the changes would have been of greater value.

The book is not divided up in the usual way by different pathologic changes but dealt rather with four anatomic regions which in conjunction with descriptions of resected stomachs form the substance of five chapters. Changes with generalized distribution therefore appear in each section. Each chapter opens with a short description of the technique of an examination with a gastrocamera without fibre optics. This technique has not found wide acceptance in Scandinavia, where television fluoroscopy or direct inspection by fibre optics is considered to achieve more exact control of the position of the camera and the distention of the stomach. The description of the examination of resected stomachs fails to mention several positions which in the reviewer's opinion are of value in providing information on the afferent and efferent loops in partial gastrectomies.

The contents of the monograph reflect the disease situation in Japan which is not wholly the same as ours. Early gastric carcinoma is abundantly represented and excellently illustrated. The difficulty of differentiating without biopsy between early malignancy and an ulcer cicatrix is stressed. Gastritis the subject of much controversy receives only superficial treatment. Diseases such as malignant lymphoma of the gastric mucosa and gastric varices are not particularly uncommon in Scandinavia but are represented each by only one case. Colonies of yeast like fungi in the stomach which produce typical endoscopic appearances are not mentioned. Extragastric compression in several cases in which the cause was carcinoma of the pancreas and in one renal cyst is considered the much commoner gastric impression of the left lobe of the liver is ignored.

The atlas undoubtedly provides a long needed aid for endoscopists however. Those of relatively short experience may concentrate on photography of the whole stomach examine at leisure and compare them with typical cases in the atlas. The book should be available at all centres where gastroscopy and above all gastrophotography are practised.

Nils Gahrn Lissen

- 3 BOJZEN E, WILLI vs C M and JUDKIN M P. Angiography of pheochromocytoma. *Amer J Roentgenol* 96 (1966) 225
- 4 KAHN P C and NICKROCH L V. Selective angiography of the adrenal glands. *Amer J Roentgenol* 101 (1967) 739
- 5 KOHLER R and HOLST L R. Angiographic localization of suprarenal tumours. *Acta radiol Diagnost* 4 (1966) 21
- 6 LAGERCRAN C. Angiographic changes in the adrenal glands. *Amer J Roentgenol* 101 (1967) 732
- 7 LA VER L O and ROSENCRANTZ M. Arteriographic appearance of pheochromocytoma. *Acta radiol Diagnost* 10 (1970) 33
- 8 MALTER I J and KOHLER P R. Angiographic findings in pheochromocytoma of the organ of Zuckerkandl. *Radiology* 97 (1970) 57
- 9 MEANEY T F and BLOMGREN E. Selectiv arteriography as a localizing and provocative test in the diagnosis of pheochromocytoma. *Radiology* 87 (1966) 309
- 10 MUNSTER W, WIERNY L and PORTSMANN W. Angiographie der Nebennierentumoren. *Fortschr Röntgenstr* 104 (1966) 367
- 11 PORTSMANN W, WIERNY L and MUNSTER W. Die selektiv Nebennierenangiographie. *Fortschr Röntgenstr* 104 (1966) 150
- 12 ROSE P. Arteriography in adrenal tumours. *Brit J Radiol* 41 (1968) 91
- 13 — KALEMAN L, RUZICKA F F JR and PANKER W. Angiographic localization of pheochromocytoma. *Radiology* 86 (1966) 266
- 14 SINGER K, CZERKALA Z, CZOPIK J, LUCIAK M, MARIELLO J, SANCZAK B i ZIELINSKI J. Obecne poglady na rozpoznawanie i leczenie guzkiolaka chromochlonnego. *Pol Przegl chir* 43 (1971) 1601
- 15 STURM A J, SCHREJA H W and PUENTES F. Differentialdiagnose der erhöhten Katecholaminscheidung bei arteriellen Hypertonien. *Dtsch med Wochr* 95 (1970) 886
- 16 WERNIG G and STROPHALER W. Diagnostik des Pheochromocytoms. *Dtsch med Wochr* 96 (1971) 121

IOBLF CONTRAST MEDIA AND ADHESIVE ARACHNOIDITIS Reinvestigation of nonoperated cases

L. IJSTAM and M. ROSENGRANTZ

of any foreign material into the subarachnoid space is followed by a meningitis generally with some cellular response and increase in protein (ALPERS & MANCILL 1971) changes that are generally transitory. Permanent alterations may be produced by some agents however only contrast media in myelography may cause the development of adhesive arachnoiditis at times extensive although even transverse spinal cord syndromes have sometimes been reported. Adhesive arachnoiditis is characterized by marked thickening of the leptomeninges with infiltration by chronic inflammatory cells. It has been reported that frank vasculitis has at times led to occlusion of the penetrating spinal vessels.

PRAESTHOLM & OLGAARD (1972) discussed the histologic changes in the medulla, meninges and nerve roots that appeared within six weeks of the suboccipital injection of methiodal (Kontrast U) in 69 per cent of rabbits. These alterations were most marked in those that survived less than a week; they were generally confined to the meninges but when the infiltration was massive the nerve roots were also occasionally involved. The longer the animals survived the

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higher the frequency of leptomeningeal fibrosis i.e. the fibrous tissue in the pia and arachnoid being thicker than the dura in the same area the fibrosis caused partial obstruction of the subarachnoid space. No correlation was evident between the volume of contrast medium and the histologic changes. The injection of methylglucamine iohalamate (Conray 60) produced only mild meningeal cellular infiltration in 25 per cent of the animals. Those killed 3 and 6 weeks after myelography had no alterations in the meninges and, above all, no signs of leptomeningeal fibrosis nor were any signs of arachnoiditis present in the control animals after subarachnoid puncture but without injection of contrast medium 10 minutes to 3 weeks before they were killed.

SKALPE (1972) injected large doses of the dimer of methylglucaminiothalamate (Dimer X) intracisternally in a small series of rats that were controlled for up to 3 months. No demonstrable neuronal or meningeal changes suggestive of adhesive arachnoiditis were observed. AURIO *et coll.* (1970) recently reported 6 cases of adhesive arachnoiditis after lumbar myelography with Conray 60. Re-examination of these patients, who had not been operated upon in the meantime revealed changes of varying severity in the root pockets or the cul de sac. These reports induced a review of our material for such adverse reactions.

Material and Methods

Kontrast U Positive myelography had always been performed with *Kontrast U* until 1969. The patient lay on the affected side with the head end of the examination couch slightly raised and spinal anaesthesia was induced by the injection of 1.3 to 1.5 ml heavy lidocain (xylocaine) after which 10 to 12 ml *Kontrast U* were injected into the subarachnoid space via a needle ad modum Stenström (OD 1.0 mm). a.p. and oblique views obtained with horizontal beam were followed by laterals with the patient prone. The patient was then placed on his other side and again oblique and a.p. views were obtained with the beam horizontal. A.p. films were thus obtained with the patient lying on the left as well as on the right side. After the examination the patient rested supine with the head slightly raised for four hours and afterwards horizontal for 20 hours.

A total of 32 patients in 856 myelographies had been re-examined but had not been operated upon. 19 of these 32 were subjected to surgery after the second examination, while the remaining 13 patients were treated conservatively.

The first examination, performed with *Kontrast U* in a further patient was followed by two re-examinations, both with Dimer X but no operation was performed. Another patient was first examined twice with *Kontrast U* and then twice with Dimer-X. He was not subjected to operation until after the last examination.

Table 1

Cases examined twice, not operated upon, before the second myelography

Contrast medium at first examination	No. of re-examined cases	No. of cases with arachnoiditis
Kontrast U	32	10 (31%)
Conray 60	3	0 (0%)
Dimer X	7	0 (0%)

Two further cases were excluded from this investigation because of missing films.

Conray 60 Five ml Conray 60 were mixed with 2 to 4 ml CSF. The examination technique was essentially the same as that for myelography with Kontrast U save that spinal anaesthesia was not induced, the films obtained often included views with the patient erect with and without bending to the side while after the examination the patient rested first for 6 to 8 hours with the head end of the bed raised 45° and then for about 15 hours with the bed horizontal.

Conray 60 was used for lumbar myelography for one year (IRSTAM *et coll* 1970) during which time 152 examinations were made. Only 3 of the patients were re-examined without having had an operation in the meantime: these 3 were re-examined with Dimer X, which has been used routinely in the department for more than two years (IRSTAM 1973).

Dimer X The examinations with Dimer X were performed in essentially the same way as those with Conray 60. The first 200 myelographies were carried out with 4 to 5 ml contrast medium mixed with an equal volume of CSF. But since the definition was often less satisfactory the ratio between the volume of medium and CSF was increased to 5:2—the entire volume (7 ml) of the mixture was usually injected. Most of the examinations with Dimer X included views in the erect position. The after-care of the patients was essentially the same as that after Conray 60 excepting for the head end of the bed raised less—usually 30° instead of 45°. The patient rested for 4 to 6 hours with the bed tilted with the head-end up and then for 18 hours with the bed horizontal.

Seven of 500 cases examined with Dimer X were re-examined without preceding surgery. Four of them were operated upon after the re-examination.

Interpretation All hospital records and films of the cases re-examined by myelography were analysed jointly by the authors. The films obtained on two or more occasions were carefully compared with regard to impaired filling of root pockets, abnormalities in the appearance of the cul de sac, its position in the

Table 2

Cases with arachnoiditis at the second myelography

Contrast medium at first examination	Changes in cul de sac	Changes in caudal root pockets	Change root pocket cysts
Kontrast U	9 (3/32)	31 (10/32)	33 (2/6)
Contra 60	0	0	0 (0/9)
Dimer X	0	0	0 (0/1)

spinal canal as well as of the visibility of the nerve roots in the caudal part of the subarachnoid space. Special attention was also paid to so-called root pocket cysts, the extent to which they were filled and their appearance.

We regard impaired filling of root pockets in the cul de sac to be the basic criterion of radiologically shown adhesive arachnoiditis. In certain cases the arachnoiditis is aggravated by further changes in the cul de sac. The degree of the arachnoiditis depends on the extent and spread of these changes.

Results and Discussion

Cases operated upon for intervertebral disc disease often have myelographic changes in the caudal part of the subarachnoid space. Only myelographies of such patients as had not been operated upon before or between the examinations were therefore accepted: this was to exclude changes in the subarachnoid space not referable to myelography per se. Myelography is performed on strict indications and the frequency of surgery is high, consequently the number of cases fulfilling the above criteria was small.

The frequency with which myelographic changes developed between the first and second myelographic examination appears in Tables 1 and 2. The most common change after examination with Kontrast U was the absence of filling of the root pocket of S2 or S3. Of the 10 cases with adhesive arachnoiditis, changes of the S3 root pockets were noted in 9, in 3 cases of which it was bilateral. In addition no filling was obtained of the root pocket of S2 at re-examination in 6 of the 10 cases and then always on the same side as the nonfilled root pocket of S3: in 1 of these 6 cases the filling of the pocket of the S2 root was absent on both sides. The root pocket of S2 was shorter at re-examination than at the primary examination in 4 cases: in 2 of these the change was bilateral. No filling at all was obtained of the root pocket of S1 in one case: neither was any filling obtained of the pocket of S2 or S3 on the same side in that case. The pocket of S1 in 4 cases was shorter at re-examination than at primary myelo-

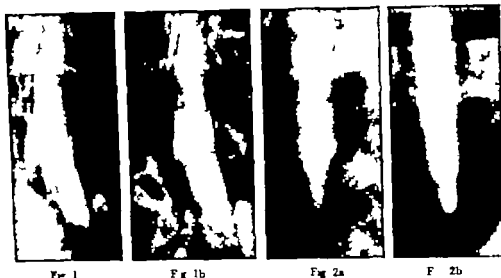


Fig 1 a) First contrast U myelography. Well defined caudal root pockets and nerv. roots
 b) Second contrast U myelography. Unfilled sacral root pockets. The S2 and S3 roots cannot be distinguished

Fig 2 a) First myelography. Conical cul de sac. Root pockets filled bilaterally and nerv. roots well demonstrated. b) Second myelography 7 months later. Rounded cul de sac 3-4 mm shorter and the S2 and S3 root pockets were unfilled on the side first examined. At each investigation sacral nerv. roots on that side were not demonstrable

graphy. In all these cases corresponding changes were evident in the root pockets of S2 and no filling at all of the root pocket of S3.

Thus changes had developed in the pocket of S3 root in 9 cases, S2 in 10 and S1 in 5 cases. If absence of a filling of a root pocket be regarded as the greatest change and a defective filling as a less marked one, it would mean that the lesions decrease in size and frequency in a cranial direction. No such changes were ever evident in the root pockets of L5. The appearances of these pockets and those of S1 were however difficult to judge because many of the cases in the group operated upon after the second examination had changes evident at myelography in the pockets around the discs between L4 and L5 and between L5 and S1 owing to herniation. Such changes in the root pockets as were thought to be caused by external compression were not included in the present investigation.

The corresponding nerve roots were also less distinct at the second examination when the filling of the root pockets was defective or missing. With no filling of the root pockets the corresponding roots were not demonstrable in the cul de sac. This may probably be taken as evidence that the arachnoiditis was not confined to the root pockets but also extended further into the subarachnoid space (Fig. 1)

some instances, to the detergents used in the cleaning of glassware, but corroboration of such a possibility in man is lacking. Some authors have also thought that it might be an allergic reaction to the anaesthetic but have produced no supporting evidence (ALPERS & MANCILL 1971).

Small local deformations of the subarachnoid space may sometimes be observed at the first myelography but may no longer be demonstrable at the repeat examination. Such changes are probably manifestations of small haemorrhages between the dura and the arachnoid due to lumbar puncture. These haemorrhages or subarachnoid bleeding from the needle track may contribute to arachnoiditis. However, no unequivocal evidence is available in support of this possibility.

Myelographic changes of arachnoiditis in the cul de sac and root pockets are the same whether the subarachnoid space extends far down into the sacrum or only to the lower border of S1.

No adhesive arachnoiditis changes were evident at the first examination in the re-examined material. This implies that the changes at the secondary examination were not caused by primary disease but by the myelographic procedure. Furthermore, the site of the adhesive arachnoiditis stresses the fact that the contrast medium plays an important causative role. Once injected, the medium being heavier than CSF will descend to the lowest part of the subarachnoid space, a part that will be exposed to the highest concentration of the medium. During the examination it will be progressively mixed with CSF and thereby diluted. Resorption investigations (IRSTAM 1973) have indicated that roentgenographically demonstrable residual medium persists longest in the most caudal part of the cul de sac which is thus exposed longest to the medium.

The patients in the series were examined first lying on the symptomatic side then prone, and finally lying on the other side. The adhesive arachnoiditis occurred unilaterally and on the symptomatic side in two thirds of the patients and bilaterally in the remaining third. The changes decreased in a cranial direction.

Autio et coll. (1972) have noted a high frequency of immediate side effects at re-examination with Conray 60 and have reported involuntary tic movements or shooting pain in the buttocks or lower limbs in 3 of the 6 re-examined patients. No such complications were observed in the present series irrespective of which contrast medium was used at the first or the second examination. Neither was the frequency of other types of immediate complications higher at the repeat examination than at the first examination, thus as true whether or not adhesive arachnoiditis was present.

After conclusion of this investigation it was brought to the notice of the present authors that similar work by RADBERG & WENGBERG (1973) had revealed adhesive arachnoiditis to be common in cases primarily examined with contrast

U These authors also observed arachnoiditis in 2 of 3 cases examined with Conray 60. Similar observations have been reported by GROSSQVIST (1972).

Changes in the lowest part of the subarachnoid space after repeat myelography and operation will be the subject of a forthcoming paper (IRSTAM & ROSENCRANTZ).

SUMMARY

Thirty four cases primarily examined by lumbar myelography with contrast U under spinal anaesthesia were re-examined without having been operated upon in the meantime. The second examination revealed adhesive arachnoiditis of varying extent in 10 cases. No such changes were evident in 3 cases first examined with Conray 60. One of 9 cases examined with Dimer X and not previously operated upon, had extensive adhesive arachnoiditis on further examination. The investigation suggests that a certain time has to elapse before the adhesive arachnoiditis can be detected.

ZUSAMMENFASSUNG

Vierunddreissig Patienten, die primär mittels lumbaler Myelographie mit Kontrast U unter Spinalanästhesie untersucht worden waren, wurden ohne in der Zwischenzeit operiert worden zu sein, nochmals untersucht. Die Nachuntersuchung zeigte eine adhäsive Arachnoiditis in unterschiedlichem Ausmass bei 10 Fällen. Derartige Veränderungen fanden sich nicht bei 3 Fällen, die zuvor mit Conray 60 untersucht worden waren. Ein Fall von 9 Dimer X untersuchten und zuvor nicht operierten Fällen hatte eine ausgedehnte Arachnoiditis bei einer späteren Untersuchung. Die Untersuchung deutet darauf hin, dass eine gewisse Zeit vergehen muss, bis eine adhäsive Arachnoiditis entdeckt werden kann.

RÉSUMÉ

Trente quatre malades examinés une première fois par sacrocaudalographie avec le Kontrast U sous anesthésie rachidienne ont été réexaminés sans à leur intervalle. Le deuxième examen montre une arachnoïdite adhésive d'importance variable chez 10 malades. Il n'y avait pas d'arachnoïdite dans 3 cas examinés le premier avec Conray 60. Un des 9 cas examinés avec le Dimer X qui n'avait pas eu d'arachnoïdite adhésive étendue à un deuxième examen. Cette étude fait penser qu'il faut laisser écouler un certain temps avant que l'arachnoïdite adhésive soit détectée.

REFERENCES

- ALPHEE B. J. and MANGALL E. L. Clinical neurology. Sixth edition. 1971. Publications Oxford 1971.
- AUTIO E., SLOLAKIN J., NORRBACK S. and SLÄTIS P. Adhesive arachnoiditis. Myelography with meglumine iohalamate (Conray). Acta radiol. Diagn. 1972.
- GROSSQVIST S. Personal communication (1972).
- DUMPE R. D. and VANDAM L. D. Long term follow up of patients with spinal anaesthetics. J. Amer. med. Ass. 156 (1954): 1486.
- IRSTAM L. Side effects of water-soluble contrast media in lumbar myelography. Diagn. 14 (1973): 111.

- LÖNNERHOLM T, SUNDBERGM M och ZIGMOND M Lumbal myelografi med Conray Meglum 282 (In Swedish) Lakartidningen 67 (1970) 3185
- and ROSENCRANTZ M Water soluble contrast media and adhesive arachnoiditis II Reinvestigation of operated cases To be published in Acta radiol Diagnosis
- KENNEDY F, SOMMER H M and GOLDBERG B R Arachnoiditis and paralysis following spinal anaesthesia J Amer med Ass 129 (1945) 664
- MOORE D C and BRIDENBAUGH L D Spinal (subarachnoid) block J Amer med Ass 195 (1966) 123
- PRAESTERL J and OLOFSSON K Comparative histological investigation of the sequelae of experimental myelography using sodium methiodal and meglumine iohalamate Neuro-radiology 4 (1972) 14
- RADDERO C and WENNERBERG E Late sequelae following lumbar myelography with water soluble contrast media To be published in Acta radiol Diagnosis
- SKALPE O I Cervical myelografi med Dimer X og Pantopaque En eksperimentell undersøkelse på rotter (In Norwegian) Paper read at the meeting of the Nordic Society of Radiology in Bergen Norway June 14 1972

LATE SEQUELAE FOLLOWING LUMBAR MYELOGRAPHY WITH WATER-SOLUBLE CONTRAST MEDIA

CLAES RADBERG and ERIK WENNBERG

Röntgenographically demonstrable late sequelae in man after myelography with the water soluble contrast media methiodal sodium (Kontrast U Conitrex) and meglumine iohalamate (Conray Meglumun 282) have hitherto been reported only infrequently. A fairly thorough search of the literature revealed only two articles describing alterations of the type termed chronic adhesive arachnoiditis (leptomeningeal fibrosis).

The first article to appear (Aurnio et coll. 1972) concerned patients who had been examined myelographically on two occasions without intervening operation. Six patients had been examined with Conray Meglumun on the first occasion and all had signs of adhesive arachnoiditis at re-examination: viz obliterated root pockets and deformation of the subarachnoid space with poor visibility of its contained roots. The changes were most prominent in that part of the space where the concentration of the contrast medium was highest i.e. most distally. The authors also mentioned a group of twelve patients who were examined first with Kontrast U; in none did a repeat examination reveal any alterations.

The second article (Bridenstam 1972) dealt with a patient in whom typical signs of chronic adhesive arachnoiditis appeared after a primary myelography

Table

Contrast U group of 21 re-examined patients and Conray group of 3 patients

	Arachnoiditis	No arachnoiditis	Total
<i>Contrast U</i>			
Same side examined	10	6	16
Different sides examined	0	5	5
Total	10	11	21
<i>Conray</i>			
Same side examined	2	1	3

with Kontrast U. The author expressed the opinion that the anaesthetic might have contributed to the lesion and that infection could not be entirely excluded.

IRSTAM & ROSENCRANTZ (1972) observed adhesive arachnoiditis in about 30 per cent of patients reviewed after myelography with Kontrast U: no changes were evident with Conray Meglumine or Dimer X as contrast media.

Although adhesive arachnoiditis has thus been described only occasionally after myelography with water soluble contrast media in man, both Kontrast U and Conray Meglumine have been extensively investigated in animal experiments. Common to all of them has been that more marked histologic changes arise with Kontrast U than with Conray Meglumine. Subarachnoid injection of Kontrast U in animal experiments has invariably been followed by histologic changes with cellular infiltration of the spinal cord and meninges. Late changes of the leptomeningeal fibrous type (adhesive arachnoiditis) have on some occasions been demonstrated with Kontrast U in dogs (HARVEY & FREISBERGER 1963) and in rabbits (ZETTLER 1969; PRAESTHOLM & OLGAARD 1972). In the rabbit the chronic fibrotic changes failed to appear until at least six weeks after the injection. With Conray no changes were found neither in cats (ISCHNER 1960) nor in dogs (HEIMBURGER *et al.* 1966).

Myelographic method. Kontrast in a dose of 10 ml was used as a routine at our hospital until the end of March 1970. Anaesthesia with 2 ml Tetracain was the rule. Kontrast U was then replaced by Conray Meglumine 282 in a dose of 4 ml mixed with an equal volume of cerebrospinal fluid before injection. Until September 1971 lumbar myelographies were performed only with the beam horizontal and only the affected side was usually examined. After September 1971 the examinations have been performed with a vertical beam on a remotely controlled tilting couch. Simultaneous fluoroscopy with a TV image mixer filter is now employed and the subarachnoid space always examined on both sides.

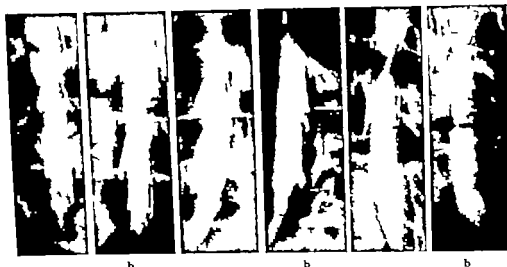


Fig 1) First examination with Kontrast U Normal myelogram b) Second examination after 2 years and 9 months Root pockets largely obliterated and deformed



Fig 2) First examination with Kontrast U Normal myelogram b) Second examination 2 years later The root pockets are partly obliterated and deformed The residual part of the root pocket at the level of the arrow is widened



Fig 3) First examination with Kontrast U Normal myelogram b) Second examination 9 years later All root pockets obliterated subarachnoid space deformed and roots no longer demonstrable in lower part

Material A total of 26 patients have been examined on two occasions by lumbar myelography without intervening operation. 23 of these patients had been examined with Kontrast U at the first examination and the remaining 3 with Conray Meglumine. Of the patients examined with Kontrast U 2 patients were excluded because the interval between the two examinations was only a week in addition to which one side had been examined on the first and the contralateral side on the second occasion. The interval between the two examinations of the remaining 21 patients ranged from 4 months to 9 years the corresponding range for the 3 patients in the Conray group was 4 months to 1 year and 4 months.

Results

The following myelographic alterations considered typical of adhesive arachnoiditis were sought (and noted): (1) obliteration of root pockets, (2) deformation of the subarachnoid space, (3) roots not demonstrable in the subarachnoid space.

Fig 4 a) First examination with Conray Meglumine Normal myelogram b) Second examination 4 months later Root pockets obliterated

Fig 5 a) First examination with Conray Meglumine Normal myelogram b) Second examination 1 year and 4 months later No demonstrable change



Fig 4

Fig 4b

Fig 5a

Fig 5b

Obliteration of root pockets was the commonest finding in the material (11 patients) followed by deformation of the subarachnoid space (11 patients). The roots could sometimes not be demonstrated in the subarachnoid space probably because adhesions had developed and fastened the roots together or to the wall of the space. This by itself was not considered to warrant a diagnosis of adhesive arachnoiditis because demonstration of the roots may be impaired by less suitable combinations of contrast concentration and exposure factors.

Ten of the 21 patients in the Kontrast U group i.e. about half presented signs of adhesive arachnoiditis at the second examination (Table). Five of the patients had one side examined on the first and the other on the second occasion and in neither could any changes be demonstrated. In the 16 patients on the other hand in whom the two examinations had been carried out on the same side changes were demonstrated in 10 patients i.e. almost two third. This difference is statistically significant (Figs 1-2-3).

All the patients in the Conray group had been examined on the same side on both occasions. 2 of these patients had changes (Fig 4) but not the third (Fig 5). Adhesive arachnoiditis is therefore not a constant finding in myelography with Conray Meglumine.

Discussion

Adhesive arachnoiditis at re-examination after lumbar myelography with Conray Meglumine was evident in the present material as in the cases reported by AURIO *et al.* Arachnoiditis was also often present after Kontrast U as op-

posed to the findings of Aurno et coll in their 12 patients owing to the absence of details in their report no explanation can be offered for the discrepancy between the results

Since arachnoiditis never occurred in the present Kontrast U material when the patient had been examined first on one side and then on the other lumbar puncture per se can hardly be held responsible for the changes. The statistically significant difference in the frequency of arachnoiditis when both examinations were made on the same side and when made first on one side and then on the other also implies that the arachnoiditis is caused by the examination and that unlike septic meningitis for example it is not a condition *suu generis*. In addition the difference between the groups suggests that a certain minimum concentration of contrast medium locally in the cerebrospinal fluid is necessary to produce arachnoiditis. This assumption is strengthened by the 6 Kontrast U cases in which arachnoiditis did not develop in spite of the fact that the examination was carried out on the same side. In 4 of these cases the concentration of contrast medium at the first examination as judged from the films, was low and only in 2 cases was of ordinary concentration. Judging from the results obtained in animal experiments and from the Conray cases in which spinal anaesthesia was not used arachnoiditis in the Kontrast U cases could not have been caused by the anaesthetic alone: the role if any played by the anaesthetic is obscure.

As pointed out by Crockqvist the myelographic alterations observed after operation because of herniation of an intervertebral disc are fairly typical. There was however the possibility that the alterations classified as postoperative might sometimes have been due to preoperative myelography if done and not to the operation.

The investigation has indicated that roentgenographically demonstrable alterations suggesting adhesive arachnoiditis often occur some time after lumbar myelography whether the examination be performed with Kontrast U or with Conray Meglumum. Whether such changes are of clinical significance is unknown. It is, however, clear that the changes are caused by a previous examination and that they substantially reduce the diagnostic information available from further myelography.

SUMMARY

Late changes of the type termed adhesive arachnoiditis proved common in patients examined by myelography with water-soluble contrast media. Ten of the 21 patients first examined with methiodal sodium (Kontrast U) and 2 of the 3 patients given meglumum sodium (Conray) presented such changes on repeat myelography.

ZUSAMMENFASSUNG

Es zeigte sich, dass Spatschaden vom Typ einer adhäsiven Arachnoiditis sich ziemlich häufig nach einer erneuten Myelographie mit wasserlöslichen Kontrastmitteln ereignen. Von 21 Patienten, die einer Kontrastmittelmyleographie unterworfen wurden, zeigten 10 Fälle solche Veränderungen nach einer Myelographie mit Natriummethiodal (Kontrast U) und 2 von 3 Fällen ähnliche Veränderungen nach Megluminothalamat (Conray).

RÉSUMÉ

Les séquelles tardives du type arachnoïdite adhésive se révèlent fréquentes chez les malades examinés par myélographie avec les moyens de contraste hydrosolubles. Dix sur 21 malades examinés la première fois avec le méthiodal sodique (Kontrast U) et 2 des 3 malades examinés par l'iothalamate de méglumine (Conray) présentaient de telles lésions à un deuxième examen.

REFERENCES

- AUTO E, SOLLAVEN J, NORRBACK S and SLATH P. Adhesive arachnoiditis after lumbar myelography with meglumine iothalamate (Conray). *Acta radiol. Diagn.* 12 (1972) 17.
- BIRSTRUP P. A case of chronic adhesive arachnoiditis after lumbar myelography with meglumine iothalamate. *Neuroradiology* 3 (1972) 157.
- CAZOTTE S. The postoperative myelogram. *Acta radiol.* 52 (1959) 45.
- FISCHER R. L. An experimental evaluation of Pantopaque and other recently developed myelographic contrast media. *Radiology* 85 (1965) 537.
- HARVEY J. P. and FRIEDBERGER R. H. Myelography with an absorbable agent. *J Bone Jt Surg.* 47 A (1965) 397.
- HEIMELINGER R. F., CAMPBELL R. L., KALINICK J. E., MEALY J. and COOPER C. L. Positive contrast cerebral ventriculography using water soluble media. *Conf. neural* 28 (1966) 97.
- IRSTAM L. and ROSENCRANTZ M. Personal communication (1972).
- PRAETTORIUS J. and OLGAARD H. Comparative histological investigation of the sequelae of experimental myelography using sodium methiodal and meglumine iothalamate. *Neuroradiology* 4 (1972) 14.
- ZEITLER E. Die Myelographie mit einer neuen Kontrastmittellösung. *Ergeb. med. Radiol.* 2 (1969) 43.

A TECHNIQUE FOR SELECTIVE VENTRICULOGRAPHY

MARIO COKRALES

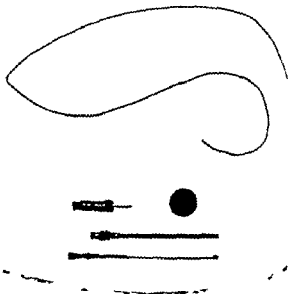
Röntgen examination of the ventricular system by means of contrast media introduced into a lateral ventricle with a needle was first described by DANDY (1918). Since then the techniques of ventriculography have been based on the introduction of needles and catheters pushed through cerebral tissue and the ventricular cavities. AZAMBUJA et coll (1956) passed a soft rubber catheter through the foramen of Monro for the selective injection of air into the third ventricle for examination of the posterior fossa.

The improvement in water soluble contrast media seems to allow injections now to be made into the ventricular system as well as into the subarachnoid space with a minimum of risk.

A new technique to facilitate selective injections into the various parts of the ventricular system is now described. This makes use of gravity to assist the manipulation of a special guide and catheter.

Method. The third and fourth ventricles are reached by the following procedure. Carotid angiography should be performed in advance to indicate the size and general configuration of the ventricular system and the location of the foramen of Monro. A burr hole is made in the calvarium approximately two

Fig 1 Instruments for selective ventriculography from box. Slightly flexible wire attached to gold chain with a rounded tip. Flexible graded catheter with reference point at tip. Adapter to syringe for injection. Small piece of rubber to maintain the cannula in position. Graded cannula mandrin with rounded tip. Flexible graded soft catheter with heavy tip and side hole as alternative for catheterization of the third ventricle through the foramen of Monro.



centimetres in front of the coronary suture, two centimetres from the midline. This distance may slightly vary depending on the size of the ventricle, shorter with small ventricles and longer in hydrocephalus. The patient is placed in a rotating chair with the head erect and the Frankfurt line horizontal. The chair should allow somersaulting as well as axial rotation.

A cannula with a mandrin with a soft rounded tip (Fig 1) is introduced into a lateral ventricle just above the foramen of Monro. The tip of the cannula should be directed towards the external auditory meatus or immediately medial to it and a few degrees towards the midline. The mandrin is removed to permit a little cerebrospinal fluid to escape and so verify the location of the cannula in the ventricular cavity. The tip of the cannula must be kept as close to the wall of the lateral ventricle as possible; unnecessary loss of CSF should be avoided. The position of the cannula may be roughly monitored.

A gold chain (Fig 1) with a rounded tip and a fairly stiff guide wire at the other end is passed through the cannula until it reaches the ventricular cavity (Fig 2). The course of the chain is controlled by monitoring and directing gentle movements of the head of the patient. The chain is passed through the foramen of Monro by tilting the head a little towards the contralateral side, rocking it gently forwards and backwards as the chain goes down through the foramen. When sufficient of the chain has been collected in a suitable position in the third ventricle to allow further manipulation, a soft flexible graded catheter with a reference point at the tip is introduced under TV control through the cannula with the chain as guide (Fig 2 a, b, c).

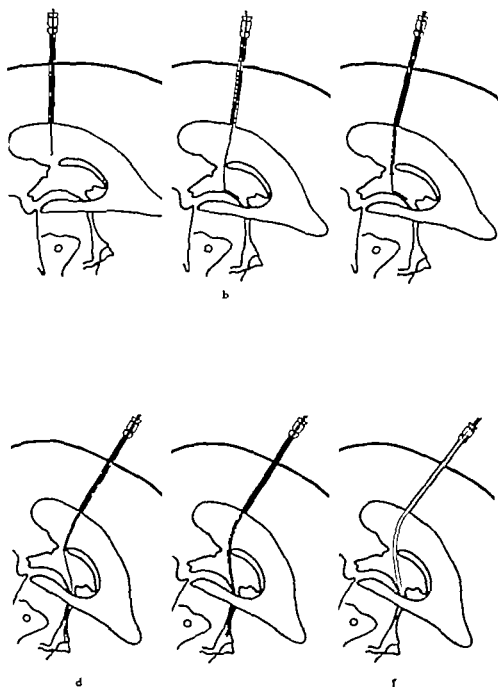


Fig. 2 Steps in the catheterization of the third (a, b) and for the (d, e) ventricles.

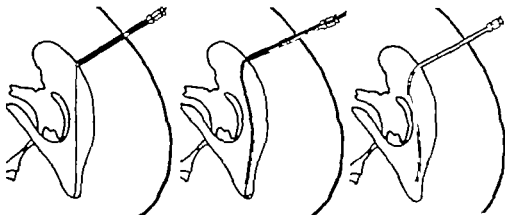


Fig 3 Catheterization of posterior part of the lateral ventricle

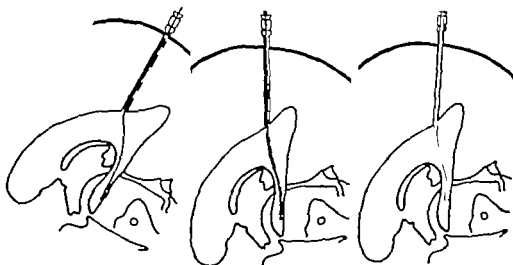


Fig 4 The hair and catheter may be introduced into the temporal horn from an occipital burr hole

If the intention is to reach the aqueduct or the fourth ventricle the catheter is allowed to remain a little below the foramen and the chain to pass through it at the same time as the head of the patient is inclined backwards this causes the chain to fall towards the opening of the aqueduct into the third ventricle. Should the chain not move freely the catheter is removed and the chain manipulated within the cannula only. The chain should then pass freely through the aqueduct (Fig 2 d). The catheter guided by the chain is advanced until it reaches the

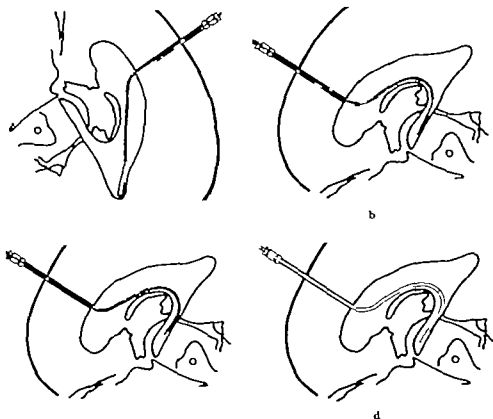


Fig 3 Alternative approaches to the temporal horn from frontal burr hole

point selected for the injection (Fig 2 c). The cannula may be removed or left in situ. The chain is then gently pulled back (Fig 2 f). A metal cannula is preferably withdrawn; a plastic cannula may remain. The position of the catheter must be checked before the injection by the withdrawal of CSF. Small injections may be made at any point. If the catheter is thin walled, soft and flexible and the chain protrudes 3 to 4 cm beyond the tip of the catheter, the system of catheter and chain can usually be manipulated as one unit.

If the region selected for the injection should be the posterior part of the lateral ventricle, the patient must lie supine immediately after the chain has reached the ventricle. It can then be guided by gravity through the body of the ventricle (Fig 3). This region may also be reached from an occipital burr hole. The chain and the catheter may easily be introduced from such a hole and guided by gravity should the region selected be the temporal horn (Fig 4). The temporal horn



Fig. 6 Clinical case. The chain was guided into the fourth ventricle (a) but the catheter failed to pass through a kink, demonstrated by injection of contrast medium into upper part of the aqueduct (b).

may also be catheterized from a frontal burr hole although this approach is less direct. The chain is allowed to collect in the posterior horn (Fig. 5 a); the head of the patient is then inclined slightly forwards and tilted towards the ipsilateral side to permit the chain to be guided by gravity to the temporal horn (Fig. 5 b). After this the catheter is advanced to its final position (Fig. 5 c) and the chain is withdrawn (Fig. 5 d).

A plastic cannula may be left *in situ* to avoid possible brain damage due to traction of the catheter. The cannula is retained in position by being passed through a small piece of rubber that fits into the burr hole; the cannula should be graded in centimetres. The catheter must be sufficiently long to allow removal of the cannula, i.e. the part outside the calvarium must be more than twice as long as the cannula.

The chain has a stiff and only slightly flexible wire attached to its proximal end to allow the catheter to be placed in position around the chain and to be guided (Fig. 1). The wire must be longer than the catheter and have the same or slightly less diameter than the chain.

A rounded tip of the chain is important for safety reasons and to improve its guiding properties. The chain must pass freely through the catheter and the catheter freely through the cannula. The catheter must be very soft and flexible to allow it to be guided by the chain; a special silicon rubber tubing has proved to be suitable. Different length and diameter of the chain, cannula and catheter may be used depending on the size of the ventricular system and the distance to the site to be explored.



b



d

Fig 7 Clinical case Oblique view. b) The chain was arrested in the third ventricle despite attempts to pass it into the aqueduct d) Selective injection of under 1 mm methyl glucamine Conray 20 demonstrated occlusion of the aqueduct

Preliminary Results

With the new technique various parts of the ventricular system were easily reached in cadavers. Three clinical cases will be described.

The chain reached the fourth ventricle in a case with a marked kink of the aqueduct (Fig 6) but beyond which it was impossible however to advance the catheter. A sufficiently soft and flexible catheter was not available at this time. The injection at the point of the kink revealed a B3-B2 (CORRALES & GREITZ 1972) right cerebellar tumour.

The second patient was a young boy who had been operated upon for a large tumour within the fourth ventricle and subsequently treated with an atrio-ventricular shunt. In spite of the fact that the aqueduct was obstructed the ventricular system proved to be small due to the functioning shunt. The chain and catheter could be placed in the third ventricle and the obstruction of the aqueduct was proved by means of a small quantity of contrast medium (Fig 7)

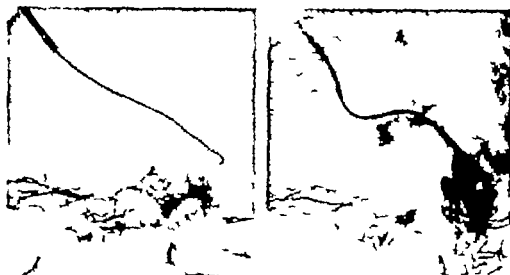


FIG. 8. Clinical case. Catheterization of the fourth ventricle. Contrast medium has passed downwards into the spinal canal (\rightarrow).

The chain is particularly easy to move in dilated ventricles and the point selected usually reached without difficulty. The chain and the catheter could thus be advanced to the fourth ventricle in a third case of a posterior fossa expansive lesion with dilatation of the third and lateral ventricle but without noticeable widening of the aqueduct (Fig. 8).

Conclusions

Selective ventriculography eliminates disturbing superimposition due to filling of cavities of less diagnostic interest and allows subtraction to be used; this is especially useful in the diagnosis of posterior fossa lesions. The method also permits the use of smaller quantities of contrast media.

The method for selective ventriculography described allows any part of the ventricular system to be reached. The natural pathways of the cerebrospinal fluid may be followed to reach the point of injection by using gravity to steer an extremely flexible guide. Hence no long tracks through cerebral tissue are followed to the third ventricle and the extremely delicate and fragile ependyma is less likely to be damaged. Dilated cavities may easily be passed and small cavities may also be explored. Injections into the aqueduct and fourth ventricle have been made for the first time through a catheter *in situ*. Management of

the patient during the procedure is easy as abrupt changes in position are not employed.

The possibility of employing a flexible catheter with a heavy metallic tip and a side hole has also been considered for the examination of the third ventricle (Fig 1).

The method presented may be used to reach structures within or adjacent to the ventricles for the purposes of biopsy, electrophysiologic recordings or stimulation and the injection of pharmacologic substances.

Patent of the method pending (Swedish Patent Application No 73 10149 5).

SUMMARY

A technique of ventriculography utilizing gravity to manipulate special guides and catheters is described. This enables any part of the ventricular system including the fourth ventricle to be reached and injected selectively.

ZUSAMMENFASSUNG

Eine Technik zur Ventrikulographie unter Verwendung der Schwerkraft um spezielle Leiter und Katheter handzuhaben wird beschrieben. Diese ermöglicht es alle Teile des Ventrikelsystems einschließlich des vierten Ventrikels zu erreichen und selektiv zu injizieren.

RÉSUMÉ

Description d'une technique de ventriculographie utilisant la gravité pour diriger des guides et des catheters speciaux. Ceci permet d'atteindre et d'injecter selectivement n'importe quelle partie du systeme ventriculaire, compris le quatrieme ventricule.

REFERENCES

- AZARBUJA N, ARASA I R, SAYON M T and GARCIA G A. Central ventriculography. *Acta neurol lat amer* 2 (1956) 58.
CORRALLES M and GRIETZ T. Fourth ventricle. II. Tumours of the cerebellum. *Acta radiol Diagnost* 12 (1972) 241.
DODD W E. Ventriculography following the injection of air into the cerebral ventricles. *Ann Surg* 68 (1918) 4.

A DEVICE FOR ROENTGEN EXAMINATION OF LUNGS IN BEDRIDDEN PATIENTS

C G MIKAEELSSON and T ADOLFSSON

One of the problems often encountered in the care of the very ill is how to lift the patient without causing pain or to place some object, a film cassette for instance, under his back. There are on the market various types of stretchers and beds with built in cassette holders and mattresses with relatively low radiation absorption. They are suitable for examinations with vertically directed rays but when horizontal rays are to be used it is usually necessary to lift the patient up onto special pillows or some other similar arrangement in order to be able to examine the dorsal parts of the body. By doing this, a fair amount of secondary radiation from the underlying support is also avoided. Special types of apparatus for lifting patients have been tried but their usefulness in a roentgen department is still fairly limited. Difficulties are encountered, for instance in inserting the lifting gear under the patient, on account of frictional resistance.

It has however proved to be possible to obtain access to the dorsal parts of the patient by using a plastic bag one half of which is invaginated into the other half. Such a device may be used both for roentgen examinations and when

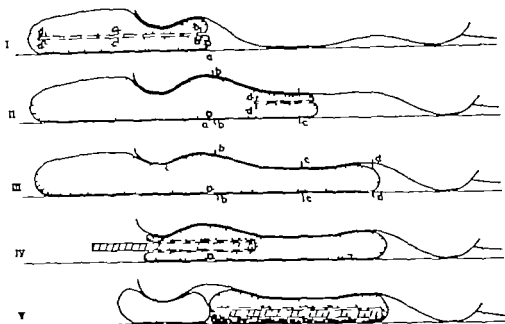


FIG. 1 Sketch showing principles of how temporarily invaginated bag unfolds under the patient and how cassette is then placed in position. The bag has been placed under the patient's head and the base of the invaginated part is located close to the shoulders I II III. When air is blown in through the valve () the invaginated part is pressed out. While at the same time each point on its wall (b c d) takes up position directly against the patient's back and the underlying support without becoming displaced afterwards IV V. The cassette is pressed in from above and the bag is invaginated again. Some of the air that has been blown in must be let out again as the volume of the bag decreases.

lifting gear needs to be introduced under the patient. If the base of the invaginated bag is placed against the patient and air is blown into it its unfolded part will be pressed in under the patient. Each section of the wall will come into contact successively and without friction with the patient's back and with the underlying support. The material does not become displaced when it begins to take the weight but only new parts of the bag roll out past those parts which have already taken up their position (Fig. 1). The only place where frictional resistance might arise would be the areas between the plastic layers inside the bag. The air pressure separates these, however. Two purposes may be achieved with a device designed along these lines. A film cassette or other such object can be placed under the patient without manual lifting and without frictional resistance. And the patient can also be lifted pneumatically for examination with horizontal beams.

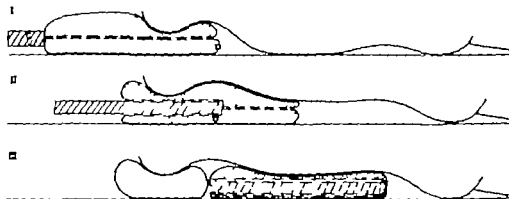


Fig. 2. Sketch showing principle underlying the permanently invaginated bag. Starting position as in Fig. 1. After small amount of air has been blown in through the valve (a) the cassette is pressed in from above. It produces an invaginated part which forces out the original one. The walls of which unfold under the patient. The inside becomes the outside while the bag is moved the length of cassette and the cassette is moved the same length.

When the bag is inflated its thickness outside the patient is considerable where it is not subjected to counter pressure. This pressure may be achieved by means of a firm surrounding frame. The frame can also serve as an attachment base for supports for both the film cassette and the patient's arms.

When the bag is completely invaginated one half of it is so rolled into the other half that the two ends come into contact. It can therefore be modified by joining them permanently. If an object is then pressed into the non invaginated end of the bag a new invaginated part will be formed which pushes out the opposite end while at the same time the whole bag moves. In this way a cassette can be introduced under the patient rapidly and easily (Fig. 2). As the cassette has to pass straight across the frame a suitable measure is to manoeuvre it with a spade.

The device. A device has been designed in collaboration with Kista (Solna, Sweden) to be used for roentgen examinations of the lungs in patients lying in bed (Fig. 3). It consists of four main parts: (1) a permanently invaginated plastic bag, (2) a cassette spade attached to the bag, (3) a flat metal frame with supports for the patient's arms and a cassette, (4) two gas cylinders with compressed air tubes and valves.

The plastic bag can take a cassette measuring 35 cm \times 35 cm and is made of soft plastic material which is reinforced with a network of nylon. The meshes are squared each side measuring 5 mm. The opening for filling and emptying is on one of the long sides, and a fixing cuff runs around the bag on a level with

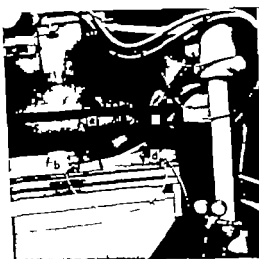


Fig 3



Fig 4

Fig 3 The complete device for examining the lungs in patient lying in bed consists of the following components: A metal frame (a) with permanently invaginated plastic bag (b). The cassette spade (c) is attached to the non invaginated end of the bag (starting position). The al (d) is connected both to the base of the invaginated bag at the other end of the frame and to the tube containing compressed air. The arm and cassette supports (e) have been lifted up. The shutter on the frame is open and the handle of the spade bent to avoid an imaginary bed head.

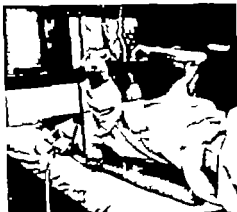


Fig 4b

Fig 4 Examination of patient in bed (a) With vertically directed beam. The bag is still only moderately inflated and has been introduced under the patient with the cassette spade whose handle can be glimpsed at the upper end of the frame. (b) With horizontal beam. The bag has been introduced with an empty spade and inflated so that the patient lies at the level of the upper edge of the cassette. The patient's arms are resting passively in the supports which also hold the vertically positioned cassette.

the valve. These details retain their position on the outer side of the bag in respect of the direction from which it is invaginated (Fig 4).

Collapsible arm supports with holders for a vertically placed cassette have been mounted on the sides of the frame. This has an opening at both ends, the

sure of one of which can be regulated. The plastic bag is introduced into the frame and is fastened at the fixed opening towards which the base of the invaginated part is directed. The cassette spade is fastened in the opposite part of the bag. The two cylinders contain 1 m³ kg of compressed air which in each case is sufficient for 100 examinations.

The roentgen examination. The metal frame is placed under the patient's head so that the base of the invaginated part of the bag is turned towards the shoulders. The bag is inflated slightly so that the cassette spade can slide easily when it is pushed from the head end of the frame into the bag. At that end of the frame, a shutter can be arranged so that the spade can be bent to avoid the head of the patient's bed. The handle of the spade is similarly jointed for the same reason. When the cassette has been placed in position the air may, if desired, be evacuated from the bag but this is hardly necessary. For the rest, the short distance between the patient and film reduces the secondary radiation and there must be some air in the bag when the cassette is pulled out again.

When the examination is to be performed with horizontal direction of the beam the patient's arms should first be placed on the supports and the cassette is then fixed to one of the arm supports. With the help of the cassette spade which is now without the cassette, the bag is once again introduced under the patient and is then inflated still further until the patient's chest rests to the upper part of the cassette. Female breasts should be fixed on top of the chest. When the examination has been completed the bag is partially deflated and is then drawn back into the frame with the aid of the spade.

In order to facilitate storing the cassette spade can be folded and fastened underneath the frame without needing to be loosened from the bag. The handle can also be folded up.

Discussion

The plastic material has low radiation absorption and is not visible at all if it is placed, during the exposures, in a double layer with the edge folded in in front of the cassettes.

In principle the plastic bag can be introduced under the patient from two directions. If it is narrow it can be readily introduced from the side. Other hoisting tackle can also be applied in this way. A wide bag however involves a considerable twisting factor which is only slightly lessened by the use of a metal frame such a frame is furthermore, in the way in examination with a horizontal beam. These disadvantages can be avoided if the bag is introduced from the head end of the patient's bed in which case the frame is placed under the patient's head.

In the early developmental work on the device the cassette was placed directly in the invaginated part of the bag and was pushed out under the patient before the bag. Its unprotected edge tended to scrape against the spinal processes especially if the patient was thin. It was found that a more suitable measure was to inflate the invaginated part first and then introduce the cassette through the opposite end of the bag. When vertical direction of the beam is used the compressed air in a bag, that is degenerated acts as an active driving force. A large volume of air is needed, and this must also be altered during each phase of the work. In addition the bag must be invaginated by hand after the examinations. If it is permanently invaginated on the other hand the air only serves to separate the walls. A much smaller volume of gas is needed and the volume can be kept constant. Also in examinations with a horizontal beam a relatively small amount of air is needed to lift the patient.

The patient's arms are fixed by their own weight in the arm supports of the metal frame. Parotic arms also rest securely and the patient's whole position is stabilized.

The device is equipped with two tubes of compressed air in order to avoid unexpected break-downs. The tubes can be placed on a roentgen stand or on the roentgen apparatus if it is of the mobile type and the other part of the equipment can also be placed there.

The plastic bag is strong and can be used for many examinations without becoming perforated. The fine nylon meshwork limits the size of any puncture that happens to arise so that it can be repaired easily with special adhesive tape. The device greatly facilitates roentgen examination of the lungs in bedridden patients both for the patients themselves and for the staff. One person alone can carry out the examination quickly without physical exertion and without causing fatigue to the patient. Exact centering can be achieved in a simple way also in the case of oblique positions. As the chest is lifted from the underlying support and is surrounded by large amounts of air the secondary radiation is low also in examinations with a horizontal beam. The films obtained are of uniformly good quality.

The device is manufactured by Alfa Siemens Flen AB 171 93 Solna Sweden.

SUMMARY

A device for examination of the lungs in patients in bed is described. It stabilizes the examination both for the staff and the patient.

ZUSAMMENFASSUNG

Einer Anordnung zur Untersuchung der Lungen von bettlägerigen Patienten wird beschrieben. Diese erleichtert die Untersuchung sowohl für den Untersuchenden als auch für den Patienten.

RÉSUMÉ

Description d'un dispositif pour l'examen radiographique des poumons chez des malades couchés. Il facilite l'examen aussi bien pour le personnel que le malade.

VOLUME CHANGES OF THE LEFT VENTRICLE DURING ACUTE MYOCARDIAL ISCHAEMIA IN DOGS

N E AHLBERG and T SREMAN

The dynamics of the ischaemic myocardium have received much attention in recent years (SONNENBLICK 1962 ROSS et coll 1967 FALSETTI et coll 1970). The clinical and experimental evaluations are however made difficult by the absence of objective methods of quantitating myocardial function following coronary artery occlusion. An ischaemic muscle segment rapidly loses its normal contractility (TENNANT & WIGGERS 1935) which means local dysfunction of the myocardial wall (AHLBERG et coll 1972). This may not be revealed by methods recording the overall function of the heart as a pump since the myocardium may compensate for functional deficits (RUSHMER 1969). The contractile function of the ischaemic muscle cells seems not to be completely lost immediately following coronary artery occlusion (HOON et coll 1969). Action potentials from the ischaemic muscle cells have been recorded (TRAUTWEIN & DUELL 1956) and the enzymatic profile of these cells does not change for several hours following the development of occlusion (GUDBJARNARSON et coll 1968). In the non ischaemic part of the myocardium increased intramycardial pressure (SHENDEROV et coll 1968) and increased activity of the glycolytic and oxidative enzyme systems of the muscle cells (BRAABEN et coll 1968) may often be recorded indicating

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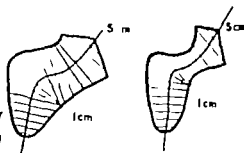


Fig. 1. Diagrams of the left ventricle cavity in end diastole and end systole with the midline 'S' and perpendicular diameters (1) drawn at intervals of 0.5 cm.

increased function also suggested by Hood & Whiting (1968). The output of the left ventricle during acute myocardial ischaemia should therefore result from contraction of a myocardial segment of normal, decreased or increased activity.

This composite ventricular function during myocardial ischaemia may be investigated by cineangiographic methods for volume determinations in different phases of the heart cycle and for the recording of the shape and motion pattern of the left ventricle (AHLBERG *et coll.* 1972). One problem is that the ventricular cavity assumes an asymmetric shape during acute ischaemia (AHLBERG *et coll.* 1972) for this reason the methods commonly used for volume estimations (DODGE *et coll.* 1960; ARIMSSON 1961) cannot be considered valid since these require that the cavity can be approximated to an ellipsoid.

The aim of the present investigation was to investigate the volume changes of the left ventricle during acute myocardial ischaemia in detail by a method that compensates for changes in the shape of the cavity (AHLBERG *et coll.* 1973). Moreover, an attempt was made to evaluate separately the function of the ischaemic and non ischaemic parts of the myocardium.

Material and Methods. The results were obtained from experiments in 13 dogs weighing 17 to 25 kg. The heart was exposed through a left-sided thoracotomy and short sections of the left anterior descending coronary artery were dissected free for subsequent occlusions with snares. Metal indicators were sutured to the epicardium centrally in the probable ischaemic areas to facilitate proper identification in the roentgen recording system. The peridium and the thoracotomy were then closed and the snares brought out through the chest wall.

Cineangiography was performed immediately after surgery with the animal placed on the left side slightly tilted so that the area of the left ventricle marked by the metal indicator was depicted tangentially by the vertical roentgen beams. The cineangiograms were recorded at 60 frames per second. The first recording was made before the coronary artery occlusion whereas the second and third

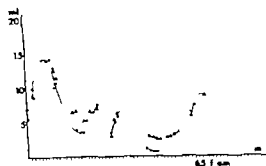


Fig. 2. Volume curves of the left ventricle constructed from every frame recorded during one heart cycle before ● and during ▲ occlusions of the left descending coronary artery. A represents the total ventricle and B and C the apical basal parts respectively.

were performed at 2 to 5 and 10 minutes; angiographic recordings were obtained at 10, 20 and 30 minutes after the latter was released. The arterial occlusions were consistently checked by ECG and in some experiments with selective coronary angiography. The electrocardiograms and the pressures in the ascending aorta, left ventricle and left atrium were obtained simultaneously with the angiograms and registered with an optical electrocardiograph (Elema Kliniek). Mean pressures were recorded by electrical integration.

The hearts were excised at the end of the experiments. Injection of Heaton fast green (Ciba) into the anterior descending coronary artery proximal to the occlusion was made to facilitate the delineation of the ischaemic part of the myocardial wall. This part was cut out and weighed and the approximate size of the ischaemia calculated as a percentage the total left ventricular weight.

The cineangiograms were examined frame by frame and the volume of the ventricle calculated from the image of the contrast filled cavity by a method previously described (AHLBOM et coll. 1973). The midline (S) was constructed on the tracings of the left ventricular cavity and diameters (I) were drawn perpendicular to it at intervals of 0.5 cm (Fig. 1). The relation between the squared length of the diameters and the midline was obtained graphically in a coordinate system and the corresponding area (A) estimated planimetrically.

The ventricular volume (V) was calculated from the formula $V = \frac{\pi}{4} \times A$ (AHLBOM et coll. 1973). The diameter through the middle point of the ventricular midline (S) was used to divide the ventricular cavity into an apical and a basal part and the corresponding volumes were estimated separately with the above formula.

The material was handled with this method as follows. In four experiments volume curves were constructed from estimations of the ventricular volume from every frame recorded during one heart cycle and similar volume curves con-



Fig. 3. Pressure-volume loops from the left ventricle before \circ \circ and during \bullet \bullet occlusion of the left descending coronary artery.

constructed from the apical and basal parts of the cavity. By drawing a tangent on the ejection portion of the volume curves the maximum rate of ejection was calculated and corrected for changes in ventricular size by dividing it by the end diastolic volume expressed in vol/s (Hoon et coll. 1968).

The external work of the left ventricle was determined in the same experiments by plotting the pressure and volume graphically for each single cardiac cycle as a loop. The area PI of that part of the loop representing the ejection phase was estimated planimetrically (Fig. 3). The pressure-volume work (PIH) was expressed as $PIH = PI \times H$ where H is a constant for conversion from mm Hg to gM \times specific gravity of blood.

The volume changes of the ventricular cavity at end diastole and end systole were examined before and 2 to 5 minutes after coronary artery occlusion. End diastole and end systole were defined as the images immediately before the closure of the mitral and aortic valves respectively. The stroke volume was obtained by subtracting the end systolic from the end diastolic volume. The ratio of the stroke volume to the end diastolic volume was calculated and termed the systolic ejection fraction. The volume changes were recorded from the total cavity as well as from the apical and basal parts separately.

The material could be divided into two groups: the first included 10 experiments with small changes in the stroke volume (≤ 10 per cent) and the second consisted of 7 experiments in which a large drop in the stroke volume (≥ 20 per cent) occurred during occlusion.

The end systolic volume, the stroke volume and the systolic ejection fraction were recorded before, during and after occlusion of the coronary artery in the total material.

The changes in the hemodynamic parameters were correlated to the relative size of the ischaemic region in all experiments.

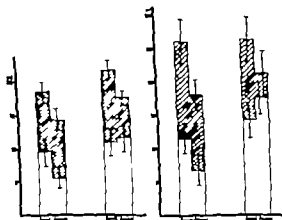


Fig 4

Fig 4 Left ventricular volume of the first group before () and during (hatched) occlusion of the left descending coronary artery separated into a basal and an apical part. Striated areas represent the stroke volumes.

Fig 5 Left ventricular volume of the second group before () and during (hatched) occlusion of the left descending coronary artery separated into a basal and an apical part. Striated areas represent the stroke volumes.

Fig 5

Results

The volume curves corresponding to the maximum and reduced ejection phases were less steep during occlusion than before indicating a decreased ejection rate (Fig 2). This difference was more marked when the volume curve was constructed for the apical part of the cavity only. The maximum ejection rate decreased from 6.60 vol/s (SE 0.08) to 4.37 vol/s (SE 0.24) during coronary occlusion and calculated from the apical part only the ejection rate decreased from 8.26 vol/s (SE 1.23) to 4.26 vol/s (SE 0.39). The corresponding curve from the basal part disclosed no obvious changes during occlusion. No consistent differences in the shape or duration of those parts of the volume curves corresponding to the isovolumetric contraction or relaxation phases were evident.

The pressure-volume loop was displaced to higher volume values during coronary occlusion (Fig 3). No obvious changes were, however, present in the shape of the loops and the pressure-volume work calculated from the loops before and during occlusion revealed no significant differences calculated from the total cavity (19.0 gMl SE 3.8 and 19.3 gMl SE 3.6) or from the apical or basal parts.

The first group had a mean ischaemic region of 19.7 per cent (SE 3.0) of the left ventricular weight. The end diastolic volume increased from 32.7 ml (SE 5.9) to 39.0 ml (SE 5.9) uniformly in the apical and basal part (Fig 4). The end systolic volume rose from 15.0 ml (SE 3.6) to 22.1 ml (SE 3.9) mainly due to the changes in the apical part, whereas the basal part presented only a small volume increase. The total stroke volume was maintained by the fact that the stroke volume corresponding to the basal part increased directly with the decrease in that of the apical part.

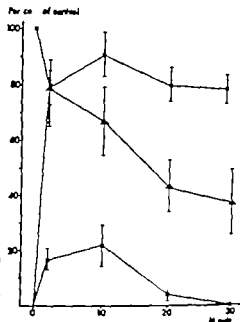
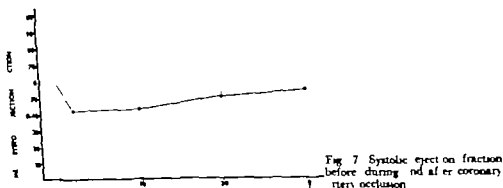


Fig. 6. Changes in per cent of control in end diastolic \circ , end systolic Δ and stroke volumes \blacksquare during and after occlusion of the left descending coronary artery. The value of stroke volume before occlusion has been given as 100 per cent and the changes during occlusion related to this.

In the second group the mean ischaemic region was 25.3 per cent (SE 1.6) of the left ventricular weight. The end diastolic volume did not change significantly during occlusion compared to the values before (44.2 ml (SE 5.3) and 47.5 ml (SE 6.1) respectively) while the end systolic volume increased from 18.3 ml (SE 3.5) to 32.1 ml (SE 4.8) (Fig. 5). As in the first group the apical part increased far more than the basal part. The total stroke volume decreased from 25.9 ml (SE 2.7) to 15.4 ml (SE 3.2) due to a decrease in both the apical and basal parts.

The end diastolic volume in the total material increased moderately during occlusion but soon after its release returned to almost the same values as before. The maximal increase in the end systolic volume was recorded as early as 2 to 5 minutes after occlusion and no further changes occurred during the rest of the occlusion period (Fig. 6). After release of occlusion the end systolic volume somewhat decreased but still remained moderately increased even 20 minutes later. The stroke volume was significantly decreased during the occlusion period and remained obviously reduced even 20 minutes after release of the occlusion (Fig. 6).

The systolic ejection fraction decreased from 0.60 (SE 0.03) before occlusion to 0.42 (SE 0.03) and 0.43 (SE 0.04) after 2 to 5 and 10 minutes of occlusion respectively. It was still significantly decreased 20 minutes after release (Fig. 7).



The correlations between the size of the ischaemic region and the changes in end systolic volume and systolic ejection fraction were statistically not quite conclusive (Fig. 8). An obvious tendency existed however for a larger ischaemic region to produce a larger increase in end systolic volume and a more marked decrease in the systolic ejection fraction especially when the effect of two unequal ischaemic regions were compared in the same animal.

Discussion

Coronary artery occlusion is followed by impaired myocardial performance (CASE et coll 1954; WEORIA et coll 1954) although it has been reported both clinically and experimentally that the hemodynamic measurements may fall within the normal range (RUSHMER 1964). The more advanced methods with force velocity analysis of ventricular function are not generally applicable in the presence of myocardial infarction due to the disparate contractile behaviour of ischaemic and non ischaemic muscles. Investigations into the configuration and volume changes of the ventricular cavity may however give valuable information as the deterioration in myocardial contractility following coronary occlusion changes the shape of the ventricular cavity (AHLBERG et coll 1972). For this reason it is important that the technique for volume estimation should compensate for different shapes of the ventricular cavity. The method used in the present investigation evidently has this quality provided that certain assumptions be made as stated in a previous report (AHLBERG et coll 1973). Further information on function would be achieved if the method allowed an estimation of the volume from different parts of the ventricle i.e. the ischaemic and the non ischaemic portions separately. This was possible with the method used and the dimensions of myocardial lesions following ischaemia could be accurately

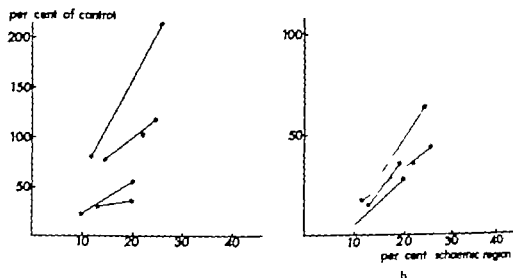


Fig. 8. Changes in two hemodynamic parameters of the left ventricle during occlusion of the left descending coronary artery as per cent of control correlated to the ischaemic region as per cent of the left ventricular weight. In four dogs experiments were performed with both a small (●) and large (○) ischaemic area. a) End-systolic volume. b) Systolic ejection fraction.

determined in the present investigation although the ischaemic occlusion of the ventricular wall failed accurately to coincide with the apical part of the cavity.

As for all angiographic methods objections can be raised to their validity for the correct demonstration of hemodynamic events. Among factors that may interfere significantly with the true existing conditions mention may be made of the effect of the sudden injection of a relatively large volume of contrast medium, the pharmacodynamic effect of the contrast medium itself and the possibility of its varying distribution within the ventricular cavity. The conclusions in the present investigation have however been made from sequential series of experiments in the same individual animal before, during and after coronary artery occlusions with a standardized angiographic and injection technique in which the error due to the above mentioned factors should have been of similar magnitude.

The increase in the end systolic volume of the ventricle during coronary artery occlusion was due mainly to the changes in that part of the cavity corresponding to the ischaemic part of the wall that remained more or less distended during systole. The increase in end systolic volume of the ventricle indicates a larger residual blood volume due to an impaired pump. This abnormal function of the ventricle was also reflected in a decrease in the systolic ejection fraction. The maximum ejection phase of the volume curves was less steep during coronary artery occlusion than before indicating a decreased maximum ejection rate. This

decrease must have been due to the deteriorated contractility of that part of the myocardial wall which was made ischaemic as the slope of the volume curve from the apical part of the cavity was more changed than the one from the total cavity. Moreover the slope of the basal non ischaemic part remained practically unchanged. This is in agreement with earlier experimental and clinical investigations of myocardial impairments following coronary artery occlusion (HARLEY *et coll* 1968 CHATTERJEE *et coll* 1971).

In one group of the experiments the end diastolic volume of the left ventricle increased during occlusion when compared with the controls. This dilatation of the ventricle in end diastole following occlusion should be regarded as a compensatory mechanism and not taken as a sign of cardiac failure. Since the ischaemic section of the ventricle makes it into a less effective pump, the chamber dilates to maintain the stroke volume with a minimum of increased muscle work. The pressure volume work of the ventricle therefore does not necessarily increase following myocardial ischaemia and was in fact the same before and during occlusion in this investigation. However in the present experiments the unaltered stroke volume was achieved mainly by increased contraction of the basal non ischaemic part of the ventricle. This means that this part of the ventricular wall performs by means of the Frank Starling mechanism increased work to compensate for the deteriorated function of the ischaemic muscle. It is therefore evident that effective cardiac output can be maintained with the heart rate essentially normal during an acute ischaemia provided that the ischaemic myocardial section does not involve too much of the ventricular wall. Such increased activity of non ischaemic muscle has been suggested from other experimental data (HOOD & WHITING 1968, SHENKEROV *et coll* 1968).

In the other group of experiments with a larger ischaemic area, no measurable dilatation of the ventricle in end diastole during occlusion was present. The stroke volume in this group was considerably reduced. The adaptive mechanism of the heart in these experiments was thus insufficient which may depend at least partly on the fact that the area of the muscle wall made ischaemic was large.

The ventricular function seemed to improve to some extent soon after release of occlusion. This indicates that impairment of the heart following short term occlusion may be reversible, although it is remarkable that even 20 minutes later the ventricular pumping function was impaired despite instantly restored coronary blood flow (LEIDER 1966). This could be ascribed to cellular changes developing acutely in the muscle.

The material failed to indicate definite correlation between the size of the ischaemic area and the increase of ventricular volume in end systole or decrease of systolic ejection fraction during coronary artery occlusion. An obvious

tendency in that direction however existed particularly when the effects of two unequal ischaemic areas in the same animal were compared. A certain correlation thus seems to be established between the extent of an acute ischaemia and the impairment of the pumping function of the ventricle at least in the same individual.

The conclusion is drawn that cineangiography may be a useful method for evaluation of the function of the left ventricle in acute ischaemia and for the differential assessment of the activities of the ischaemic and non ischaemic part. If cineangiography could be performed in the acute stage of myocardial infarction a way of evaluating functional impairment after coronary artery occlusion in man might be opened.

Acknowledgement

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SUMMARY

Volume changes of the left ventricle during acute myocardial ischaemia have been investigated in dogs. The volume of the ventricular cavity and its separate parts were estimated from single plane cineangiograms. The hemodynamic changes following coronary artery occlusion could be related to the ischaemic region. The drop in function of the ischaemic part of the myocardial wall seems to be compensated for by increased activity of the non ischaemic part.

ZUSAMMENFASSUNG

Volumenänderungen des linken Ventrikels während akuter Ischämie des Myokards wurden bei Hunden untersucht. Das Volumen der ventrikulären Kavität und deren einzelner Teiler wurden von einer Ebene hergemessenen Filmangiogrammen bestimmt. Die hämodynamischen Veränderungen nach Verschluss der Koronararterie konnten zu den ischämischen Abschnitten relationiert werden. Der Abfall in der Funktion des ischämischen Teil der Myocardiand scheint durch gesteigerte Aktivität des nicht ischämischen Teils kompensiert zu werden.

RÉSUMÉ

Les auteurs ont étudié sur des chiens les modifications de volume du ventricule gauche au cours d'ischémie myocardique aiguë. Le volume de la cavité ventriculaire et de ses différentes parties a été estimé par l'emploi de cinéangiographies unidirectionnelles. Ils ont pu établir un rapport entre les modifications hémodynamiques dues à l'occlusion de l'artère coronaire et la région ischémique. La déficience fonctionnelle de la partie ischémique de la paroi myocardique paraît compensée par une activité augmentée des parties non ischémiques.

REFERENCES

- AMLERO N E, PALLEY S and SHERMAN T. Left ventricular changes during coronary artery occlusion in dogs. *Acta radiol. Diagnosis* 12 (1972) 789
- AMLERO N E, FRITTEVENO L, LINDFORS M and SHERMAN T. Cineangiographic estimation of the left ventricular volume during acute myocardial infarction in dogs. *Acta radiol. Diagnosis* 14 (1973) 43
- ARIMONDO H. Angiocardiographic determination of left ventricular volume. *Acta radiol* 56 (1961) 321
- BRAAMCH W G, JARJASVO S, PULP, RAJENDRAN G and BING R J. Early changes in energy metabolism in the myocardium following acute coronary artery occlusion. *Circulat Res* 23 (1968) 479
- CASE R B, BERGLUND E and SARNOFF S J. Ventricular function II. Quantitative relationship between coronary flow and ventricular function with observations on unilateral failure. *Circulat Res* 2 (1954) 319
- CHATTERJEE K, SACCOMI M, SUTTON G C and MILLER G A H. Assessment of left ventricular function by single plane cineangiographic volume analysis. *Brit Heart J* 33 (1971) 563
- DOUGHERTY H T, SANDLER H, BALLEW D W and LORD J D. The use of biplane angiocardiography for the measurement of left ventricular volume in man. *Amer Heart J* 60 (1960) 762
- FALSETTI H L, MATHE R E, GRANT C, GREENE D G and BUNNELL I L. Left ventricular all stress calculated from one plane cineangiography. *Circulat Res* 26 (1970) 71
- GURJARANIAN S, BRAAMCH W, COVATY C and BING R. Metabolism of infarcted heart muscle during tissue repair. *Amer J Cardiol* 22 (1968) 360
- HARLEY A, BEHAR V S and MITCHELL H D. Immediate hemodynamic effects of acute coronary occlusion and their modification by anesthesia. *Amer J Cardiol* 22 (1968) 559
- HOOB JR W B and WHITING R B. Experimental myocardial infarction—increased fibre shortening in non infarcted muscle. *Clin Res* 16 (1968) 514
- , RAGGLEY C E and ROULETTE E L. Ejection velocity and ejection fraction as indices of ventricular contractility in man. *Circulation* 38 (1968) Suppl No 6 p 101
- , COVILLI V H, ABELMAN W H and NORMAN J C. Persistence of contractile behaviour in acutely ischaemic myocardium. *Cardiovasc Res* 3 (1969) 949
- LINDER E. Studies on coronary collateral blood flow in dogs by Krypton⁸¹ and Xenon¹³³ clearance. *Elanders Boktryckeri AB Gøteborg* 1966
- ROSS JR J, COVILLI J W and SONNENBLICK E H. The mechanics of left ventricular contraction in acute experimental cardiac failure. *J clin Invest* 46 (1967) 299
- RUBINER R F. Function of infarcting myocardium. *Circulation* 39 (1969) 168
- SHENDEKOV S M, TARASOVA G, MOTARADZE Yu S and MIKHAYLOV F Z. Contractile function of undamaged parts of the left ventricle after acute disturbances of the coronary circulation. *Bull Akad Med Sci* 63 (1968) 34
- SONNENBLICK E H. Force-velocity relations in mammalian heart muscle. *Amer J Physiol* 204 (1962) 931
- TAYLOR R and WIGGERS C. The effect of coronary occlusion on myocardial contraction. *Amer J Physiol* 112 (1935) 331
- TRAUTWEIN W and DÜDEL J. Aktionspotential und Kontraktion des Herzmuskels im Sauerstoffmangel. *Plügers Arch ges Physiol* 263 (1956) 23
- WEIGER R, FRANK C W, MISHRA G A, WANG H H, MILLER R and CASE R B. Immediate hemodynamic effect of acute coronary artery occlusion. *Amer J Physiol* 177 (1954) 123

ANOMALOUS ORIGIN OF THE LEFT CORONARY ARTERY INDIRECTLY DEMONSTRATED BY RADIOANGIOGRAPHY

W. MORTENSSON and N. R. LUNDSTROM

An anomalous origin of the left coronary artery from the pulmonary artery usually causes signs of serious heart disease during the first months of life. The electrocardiogram reveals evidence of ischaemia and infarction of the left ventricle with enlargement of the left ventricle and atrium at roentgen examination. Similar clinical, electrocardiographic and radiologic changes may also be present in endocardial fibro-elastosis, different kinds of myocarditis, glycogen storage disease, thrombosis of the coronary artery and arteriovenous shunts involving the left coronary artery (GOLDBRODER 1960; SARBSTON et coll 1960; MOSS & ADAMS 1968).

Supraventricular aortography usually produces the correct diagnosis. When an anomalous origin of the left coronary artery is not obvious, catheterization is performed on the right side of the heart and the contrast medium injected into the right ventricle or the pulmonary artery. These procedures frequently yield the most information and may disclose the artery, as will be described.



b

Fig 1 a) Cardiocatheteriography of the right ventricle. Filling defect in contrast medium in the anterior pulmonary cusp. b) Supraventricular aortography (late phase). Contrast medium still remains in the dilated right coronary artery. Retrograde filling of the left coronary artery and the anterior pulmonary cusp.

Case report

Three unrelated infants with heart disease. One had spells of restlessness, pallor, sweating and crying at the age of 6 weeks and 2 weeks later developed congestive heart failure. The other 2 had congestive heart failure at the age of 3 months and 4 months respectively. Myocardial ischaemia and infarctions were evident at ECG. Roentgen examination of the chest revealed enlargement of the left ventricle and atrium with the pulmonary vessels somewhat dilated compatible with left to right shunt. Catheterization of the right side of the heart and cardiocatheteriography were performed when the infants were 2 to 3 months old. They were recatheterized when 5 and 17 months old respectively. Supraventricular aortography was carried out when the infants were 3 months, 6 months and 2 years old respectively.

A slight admixture of oxygenated blood was present in the pulmonary artery in all cases but the blood pressure was normal. Cardiocatheteriography revealed a filling defect in the contrast medium in the posterior cusp in 2 infants and in an anterior cusp of the pulmonary artery in one (Figs 1, 2). These were thought to be caused by left-to-right shunt through coronary artery with an anomalous origin from the pulmonary artery and was later proved by aortography (Figs 1b, 2b) as also evident that the left coronary artery was filled in retrograde direction through numerous collaterals from the right coronary artery.

The patients were operated on at the age of 4 months, 1 1/2 years and 2 1/2 years respectively with ligation of the left coronary artery close to its origin from the pulmonary artery. Two are still alive and have improved considerably but one infant (the youngest) died about one month after operation from pulmonary complications (repeated infection and atelectasis).



Fig. 1. a) b) Supravulvar angiography. The right coronary artery is dilated. The left coronary artery and dorsal pulmonary artery are filled through a large patent foramen ovale over the anterior and diaphragmatic parts of the heart. c) Cardioangiography of the right ventricle. Filling defect present in the right pulmonary artery.

Discussion

The blood pressure in the aorta and pulmonary artery is the same during foetal life but falls rapidly in the latter during the neonatal period. If the left coronary artery should arise from the pulmonary artery the pressure will con-

be insufficient to maintain adequate perfusion of the myocardium. At first the collaterals between the coronaries are poorly developed in contrast to the conditions of congenital stenosis or stenosis of the proximal part of the left coronary artery. The flow in the left coronary artery is then presumably in an antegrade direction which has also been demonstrated by cardioangiography in a few 2 to 4 month old infants (TALNER et coll 1958, KEITH 1959, FRIEDENBERG et coll 1963, BOGARTYEN 1964). The blood then commences to flow from the gradually dilating right coronary artery through improved collaterals to the left coronary artery. The low resistance of the pulmonary vascular bed however produces a left-to-right shunt from the aorta through the coronaries to the pulmonary artery. Even a large central flow through the left coronary artery will consequently be inadequate for the peripheral perfusion of the myocardium supplied by the left coronary artery. The increase of oxygen saturation in the pulmonary artery is sometimes too low to afford a reliable diagnosis of shunt although this may depend upon where in the pulmonary artery the blood sample is taken. The shunt is best disclosed by angiography with injection of contrast medium into either the aorta supra-auricularly or the right ventricle.

The filling defect in the contrast medium in the pulmonary artery is best demonstrated during diastole and when the injection is made into the right ventricle. During systole or when the contrast medium is injected into the pulmonary artery the filling defect is less obvious or is absent because of a better mixing with the blood from the left coronary artery. Cinecardioangiography in one of the present cases revealed that although the blood flow in the left coronary artery was mainly in a retrograde direction the medium was forced from the pulmonary artery into the most proximal centimeters of the left coronary artery during every systole.

The filling defect earlier reported by JAMESON et coll (1963) in a 4 1/2 year old boy was present in all the 3 infants now reported with this malformation. A similar filling defect in the pulmonary artery was also observed in a patient with a small aortico-pulmonary window but was not localized in connection with the cusps. The differential diagnosis from the clinical or radiologic points of view should not present difficulties.

SUMMARY

An anomalous origin of the left coronary artery from the pulmonary artery was indirectly demonstrated by cardioangiography of the right ventricle and confirmed by supra-auricular aortography in 3 infants.



b



Fig. 1. a) Supra-lumbar right coronary artery is dilated. b) Left coronary artery and dorsal pulmonary artery filled through a large number of anterior and diaphragmatic branches. c) Ca diastereograph of the heart. d) right ventricle. Eminent defect present in the right pulmonary cusp.

Discussion

The blood pressure in the aorta and pulmonary artery is the same during foetal life but falls rapidly in the latter during the neonatal period. If the left coronary artery should arise from the pulmonary artery the pressure will soon

be insufficient to maintain adequate perfusion of the myocardium. At first the collaterals between the coronaries are poorly developed in contrast to the conditions of congenital atresia or stenosis of the proximal part of the left coronary artery. The flow in the left coronary artery is then presumably in an antegrade direction, which has also been demonstrated by cardioangiography in a few 2 to 4 month-old infants (TALNER et coll 1958 KARTH 1959 FRIEDENBERG et coll 1963 BOOKSTEIN 1964). The blood then commences to flow from the gradually dilating right coronary artery through improved collaterals to the left coronary artery. The low resistance of the pulmonary vascular bed however produces a left to-right shunt from the aorta through the coronaries to the pulmonary artery. Even a large central flow through the left coronary artery will consequently be inadequate for the peripheral perfusion of the myocardium supplied by the left coronary artery. The increase of oxygen saturation in the pulmonary artery is sometimes too low to afford a reliable diagnosis of shunt although this may depend upon where in the pulmonary artery the blood sample is taken. The shunt is best disclosed by angiography with injection of contrast medium into either the aorta supraauricularly or the right ventricle.

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SUMMARY

An anomalous origin of the left coronary artery from the pulmonary artery as indirectly demonstrated by cardioangiography of the right ventricle and confirmed by supraauricular aortography in 3 infants.

ZUSAMMENFASSUNG

Ein anomaler Ursprung der linken Koronararterie von der Arteria pulmonalis wurde indirekt durch Kardioangiographie des rechten Ventrikels nachgewiesen und durch supra-aortale Aortographie bei 3 Kindern bestätigt.

RÉSUMÉ

La cardiographie montre indirectement chez trois nourrissons, l'origine anormale de l'artere coronaire gauche qui venait de l'artere pulmonaire. Ceci a été confirmé par aortographie supra-aortale.

REFERENCES

- BOOKSTEIN J. Aberrant left coronary artery. *Amer J Roentgenol* 91 (1964) 515.
 FRIEDENBERG M., HARTMANN A., SILVERMAN J. and BURFORD TH. Opacification from the pulmonary artery of an anomalous left coronary artery. *Radiology* 80 (1963) 806.
 COHENBERG R. I. Angiocardiographic diagnosis of an anomalous left coronary artery arising from the pulmonary artery. *Amer J Cardiol* 6 (1960) 694.
 JAMESON A., ELIAS H. and LEVINE O. Anomalous left coronary artery arising from pulmonary artery. *Brit Heart J* 25 (1963) 23.
 KERTT J. The anomalous origin of the left coronary artery from the pulmonary artery. *Brit Heart J* 1 (1959) 149.
 MOORE A. and ADAMS L. Heart disease in infant, children and adolescent. Williams and Wilkins Comp. Baltimore 1968.
 SUTTON JR. D., PELLARCONO S. and LAURIE H. Myocardial infarction in infancy. *J thorac cardiovasc Surg* 40 (1960) 321.
 TALAN R. N., STEIN A. and HOLBY M. Angiocardiographic diagnosis of aberrant left coronary artery from pulmonary artery. *Circulation* 18 (1958) 788.

PREOPERATIVE LOCALIZATION OF PHEOCHROMOCYTOMA

O F AGEK J HAUDE and J LEPASOON

Pheochromocytomas are chromaffin tissue tumors and arise most commonly from the adrenal medulla. Other sites harboring suitable stem cells particularly the sympathetic chain may also furnish them substrate. Like the adrenal medulla such tumors characteristically produce vasopressor substances of the catecholamine chemical group (epinephrine and norepinephrine).

The periodic release of the substances into the blood stream in exaggerated quantity gives rise to paroxysmal hypertension. In its classical form the clinical diagnosis of pheochromocytoma is easy but sustained hypertension may make the diagnosis difficult and, further labile hypertension on other bases may mimic the effects of the tumor. Chemical or pharmacologic screening tests developed to more firmly substantiate the tumor presence include glucagon, histamine and tyramine provocation tests (causing release of catecholamines from the tumor) and tests for blocking the effect of catecholamines upon end organs (phentolamine test). These carry a significant incidence of false negative and false positive results (SHULPS 1966 HARRISON et coll 1968 SCHMID & KRAUTHHEIM 1969 SA

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Table

Result of biochemical assay to assess whole number VMA = vanilmandelic acid F = epinephrine
 NE = normetanephrine VNF = normetanephrine and radiographic examination 10 patients with 13
 histologically proven benign pheochromocytomas

Case	Age sex and m stature blood pressure	11 ghest 24 hour urine excretion of VMA or catecholamines	Peripheral enous catecholamine (normal /g/l) F < 0.5 NF < 6.0	Site and amount largest central en us cate b l muse
1	37 F 100/135	VMA - 42 mg		Lo inferior ca l en NF 20 µg/l
2	28 F 200/110	VMA 20 mg NF 90 µg NE - 5 /g		L l NE 6 /g/l
3	54 M 170/110	VMA - 40 mg		Lo inferior ca l en NF - 17 µg/l
4	37 F 250/140	VMA - normal	NE 4 µg/l F 2 /g/l	L l E 5 µg/l High af ca al en E 0 µg/l
5	44 F 200/120	VMA 18 mg NE - 226 µg		L renal NE 110 µg/L
6	42 F normal	VMA - 17 mg		L l NF 5 µg/L
7	43 F 230/110	VMA - 24 mg		I adrenal NF E 61 µg/l
8	36 F 150/100	VMA - 39 mg	NE 48 /g/l E 4 µg/l	S mjk unsuitable for lym
9	50 M 220/100	VMA - 67 mg		
10	53 F 200/120	VMA - 67 mg		

PIRA et coll 1970) and provocation tests carry also an inherent risk for the patient. The determination of the metabolic endproduct of catecholamines, vanilmandelic acid (VMA) is simple and SCHWED & KRAUTHORN (1969) consider this test to be the most reliable for pheochromocytoma when carried out

Table (cont.)

Aortographic tumor localization	Selective angiographic tumor localization	Adrenal phlebographic tumor localization	Angiographic tumor size in centimeter
Left of aortic bifurcation			7/10
L adrenal			2x4
L adrenal	L adrenal		6
Not found	L adrenal		2
L adrenal	L adrenal	L adrenal	3
R adrenal	R adrenal		6
R adrenal			R 10
L adrenal	L adrenal	L adrenal	L 1
Bilateral adrenal		Bilateral adrenal	R 12 L 3
Bilateral medial to inferior renal hila	Bilateral medial to inferior renal hila		R 6 L 6
L adrenal			8

Normal 4 hour excretion VMA < 6.0 mg NE < 150 μ g E < 50 μ g NMIE < 240 μ g

Sampling performed after extirpation of R adrenal tumor

R adrenal not examined selectively

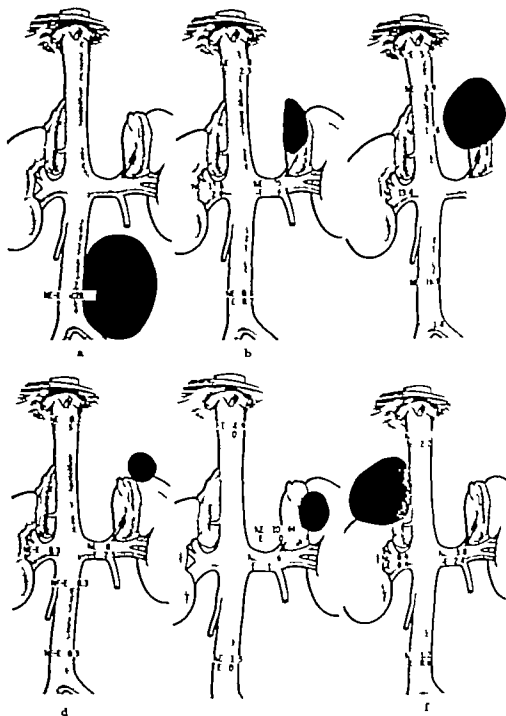


Fig. 1 (For legend see opposite page.)

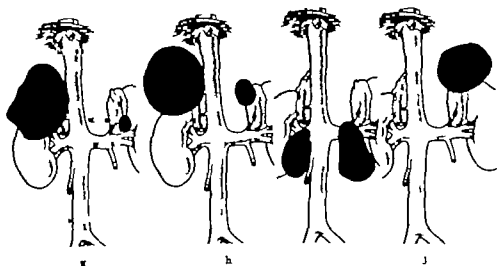


Fig. 1 Depiction of site and size of pheochromocytoma in all cases. The values of catecholamine determinations obtained at specific sites appear on the individual diagrams. Numerical values are in microgram/l. NE = norepinephrine, E = epinephrine, NE+E = combination of the two. Case 1 () precise measurement not available; measurements from both renal veins and superior portion of inferior vena cava significantly lower. Case 7 (g) left adrenal vein assay during hypertension; veins following adrenal phlebography. Control sample unsuitable for analysis. Other samples obtained before hypertension; cross all 6 1/2 months after removal of right adrenal pheochromocytoma.

by means of gas chromatography (WILLIAMS & GREER 1963). HARRISON et coll (1968) feel that direct assay of epinephrine/norepinephrine is the most successful investigation.

Biochemical establishment of the presence of pheochromocytoma in a patient, however, is not sufficient. Even a pharmacologically influential tumor may be quite small, and preoperative information about its precise site, arterial supply and venous drainage contribute materially to the ease and safety of extirpation.

Some simple radiographic examinations (survey films of the abdomen, urography or phlebography of the inferior vena cava) may be helpful in tumor localization. Potentially more useful, the retroperitoneal pneumography (MURCHER 1937) is no longer frequently employed.

In 1966 BJÖRSEY et coll from Lund reported diagnosing 5 pheochromocytoma cases by aortography or selective nephroangiography. Since we have expanded the technique to include selective angiography of more potential supplying arteries, adrenal phlebography and venous sampling of blood from the inferior caval vein, renal and adrenal veins for catecholamine determinations. Appraisal of 10 patients with 13 histologically proven benign pheochromocytomas (Table)



Fig. Case 1. Hypervascular paraneoplastic lesion of the abdominal aorta. A lesion located at this level would be only marginally depicted if entering of beam was high enough to include the upper abdomen on the film. This emphasizes the need in some patients to extend aortography to the lower abdomen. The need for such coverage may be anticipated by analysis of central venous area (Fig. 1).

illustrates the relative merits and pitfalls of these investigations. Three patients (Cases 6 to 8) had Sipple's syndrome and will be reported separately with special emphasis on this familial disease (TELFORD *et al.*).

Methods

During catheterization all patients were carefully physiologically monitored and phentolamine (Regiune, CIBA Basel) was available for prompt treatment of hypertensive crisis. Alfa receptor blocking agents were administered prophylactically in 5 patients.

Venous catheterization. In 7 patients catheterization of the inferior caval vein and renal veins for blood samples (catecholamine determination) was performed (Fig. 1). In Cases 5 and 7 aliquants were also withdrawn from the left adrenal vein. Samples from the inferior caval vein were taken at the level of L4 and above the renal veins near the level of Th 12. Venous catheterization was carried out before angiography in 4 patients and at the same session in 3 patients.

Adrenal phlebography Four tumors (1 right and 3 left adrenal) in 3 patients (Cases 5-7-8) were examined with this method, the phlebography being performed immediately after samples were taken for catecholamine determination. An amount of 4 to 8 ml of contrast medium 60 % was injected by hand and renal radiography was performed.

Aortography and selective angiography Aortography was performed in all 10 patients (40 to 50 ml contrast medium 76 %) with the catheter tip at the level of Th 12. In 3 patients a second aortic injection was made near the bifurcation to verify the presence of a tumor in the lower abdomen. Selective angiography (adrenal, renal, celiac, inferior phrenic or lumbar arteries) supplemented aortography in 6 patients (7 tumors). In 3 patients injection of contrast medium was immediately preceded by an intraarterial injection of 6 to 8 µg epinephrine (HARRY & NIKLOSZ 1967; LAUDE & AGLE 1969).

Results

The results are given in the Table. Eleven of 13 tumors were demonstrated at aortography. In Case 7 the diagnosis of left pheochromocytoma was only tentative and one tumor remained undiagnosed (Case 4).

Selective angiography was helpful in better demonstrating the tumor and its blood supply in each case so examined. One partially necrotic pheochromocytoma (Case 4) was demonstrated only by celiac artery injection following 6 µg of intraarterial epinephrine.

Adrenal phlebography demonstrated all 4 tumors so examined although one tumor of 1 cm diameter was finally diagnosed only by correlation with aortography, angiography and catecholamine assay.

Catecholamine determinations from the inferior caval vein, renal or adrenal veins indicated pheochromocytoma in all 7 cases performed, but the site of the tumor was correctly indicated in only 4. The highest catecholamine values were in samples from adrenal veins directly draining tumor. In Case 7, that of a small pheochromocytoma not definitely diagnosed by angiography or adrenal phlebography, the diagnosis and site of a hormonally active pheochromocytoma was established by high catecholamine levels in the left adrenal vein found during a transient hypertensive episode.

Complications A hypertensive crisis occurred in 3 patients during angiography—in one following aortography, one at selective catheterization (no injection) of the middle adrenal artery and one at adrenal phlebography. The first two patients were not pretreated with alpha receptor blocking agents, but their crises



a



b

Fig. 3 (For legend see opposite page)

responded promptly to intravenous administration of phentolamine. The third patient was not only pretreated but was receiving an intravenous drip infusion of 65 mg dibenzylamine immediately before and during examination. She reacted transiently to an injection of 6 ml contrast medium into the left adrenal vein, blood pressure rising from 190/100 mm Hg to 230/130 and returning spontaneously to the pre-crisis level.

Discussion

The angiographic diagnosis of more than 150 pheochromocytomas is documented in the literature. Large, well vascularized tumors present no difficulty and will be detected at aortography (Fig. 2). In an analysis of the angiographic appearance of pheochromocytoma it has been shown that the lesion may lack pathologic vasculature in the arterial phase, being distinguishable only by accumulation of contrast medium in the late capillary and venous phases (LAWVER & ROSENCRANTZ 1970). We also observed this appearance in a partially necrotic pheochromocytoma, Case 4 (KAUDE & AOKI 1969). The diagnosis of a small tumor, especially if biochemical examinations are not helpful, may be formidable. In these difficult cases a useful adjunctive method for pheochromocytoma localization is epinephrine enhancement of selective angiography.

Selective adrenal phlebography, performed first by CRANSTON (cited by BUSH & MAHER 1959), is a suitable method for detection of adrenal lesions (KAUDE & NIKROSI 1967; HARRISON et coll. 1968; REUTER et coll. 1967; SUTTON 1968; MIKELLSON 1969 and others). The phlebographic findings in our 4 cases were characterized either by displacement of adrenal veins (Fig. 3) or by rich vascularization of the tumor and its adrenal bed (Fig. 4). In Case 7 (Fig. 5) a small tumor was suggested but not definitely demonstrated. An impediment to adrenal phlebography is the variation in normal anatomy of the right adrenal veins (JOHNSTON 1957); their multiplicity and small size almost prohibiting total demonstration by selective injection of contrast medium. Nonetheless, success may be anticipated in about 70 % of the right-sided attempts (REUTER et coll. 1967; MIKELLSON 1967 to 1969) and in virtually all on the left. Rarely, anomalous adrenal venous drainage may complicate the issue (Case 3). Obviously the venous drainage of extra-adrenal pheochromocytomas (10 to 20 % of

Fig. 3 Case 8. a) Aortic injection, late arterial phase. Large, poorly vascularized right adrenal tumor outlined by stretched suprarenal arteries. Displacement of left adrenal arteries (—). b) Right adrenal phlebography. Circumferential plexus of dilated veins deflected by and draining the large adrenal tumor. c) Left adrenal phlebography. Dilated adrenal and inferior phrenic veins round the tumor in the lower pole of the adrenal gland. Phlebographic demonstration more convincing than aortography.

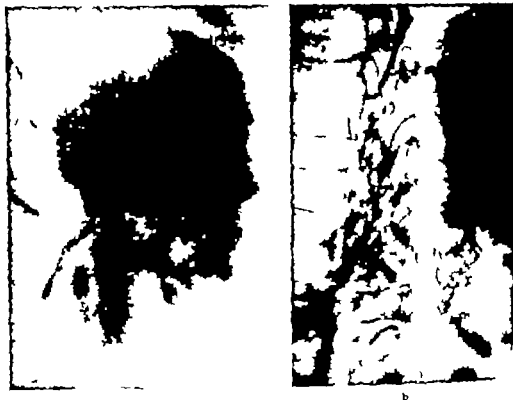
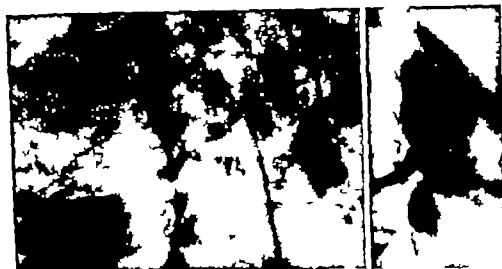


Fig. 4 Case 5. a) Selective left renal angiography. Ill-defined area (tumor) with active vascularity in the capillary phase. The tumor situated medial to and deflecting the upper pole collecting system derived its blood from renal and inferior adrenal arteries. b) Left adrenal phlebography. Multiple dilated venous channels draining the hypervascularized adrenal gland. The tumor itself rich in veins and deflection of adjacent veins as well. The indirectly lowered catecholamine values obtained from the adrenal vein (Fig. 1 c) emphasize the importance of draining the samples more selectively and lower to the tumor to avoid dilution by venous flow from other organs.

tumors more often in children) may be into the lower part of the inferior caval vein (Fig. 1 a) (v. EULER et coll. 1955). Because angiography usually will not demonstrate venous pathways from the tumor (adrenal phlebography provides valuable preoperative information. It can be performed in immediate sequence to venous catheterization for biochemical sample collection.

Central venous sampling (v. EULER et coll. 1955) is particularly important when other biochemical tests or angiographic examination fail. For example in Case 4 (VMA normal) elevated catecholamine levels in the high inferior vena cava and in the left renal vein (Fig. 1 d) focused the eventual successful angiographic search for a left adrenal pheochromocytoma into the appropriate region after two unsuccessful angiographic attempts which lacked such direction.

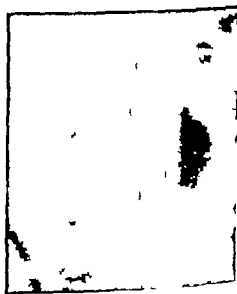


b

Fig. 5 Case 7 a) Aortography. Large relatively hypo-vascular right suprarenal tumor. Possible small hyper-vascular lesion in the left adrenal gland (→) also suggestive from phlebography. Without central cross assay the patient was operated on and the right adrenal pheochromocytoma was removed. b) Repeat left adrenal phlebography (following worsening hypertension postoperatively). 1 cm area of slight hyper-vascularity and deflection of veins in the lower pole (→). The definitive indication of hormonally active pheochromocytoma was the elevation of catecholamine levels in the sample obtained from the left adrenal vein during hypertensive crises evoked by adrenal phlebography (Fig. 1 g). Normal catecholamine levels in other veins before the crises.

Samples solely from the inferior vena cava may be misleading (HARRISON et coll. 1968) and indicate only the general level but not the side or exact site of the tumor (BRUNNER et coll. 1966; GROSS et coll. 1967). Even renal vein samples may be deceiving because of anomalous venous drainage from the tumor (v. EULER et coll. 1955) or by admixture of blood from the contralateral renal vein and inferior vena cava (Cases 2 and 3). Multiple hormonally active tumors might also complicate neoplasm localization by chemical determinations.

In fact three of our cases demonstrated misleading venous catecholamine levels in regard to tumor site. In Case 2 (left sided tumor) high catecholamine concentrations were found in both renal veins, indicating the possibility of bilateral pheochromocytomas (Fig. 1b). The right adrenal however was angiographically normal, an observation confirmed after extirpation of the left adrenal lesion by normalization of blood pressure and reversion to normal status. Presumably, mixture of venous blood from the left into the right renal vein was responsible for a high catecholamine level on the right.



b

The catecholamine determination in Case 3 indicated a low pheochromocytoma (Fig 1c). Yet, the tumor was found in the left adrenal. Collateral pathways from the left adrenal into the lower part of the inferior caval vein following a previous nephrectomy was the explanation for high levels in that part of the vein (Fig 6). The high catecholamine concentration in the remaining right renal vein was probably caused by mixture of blood from the inferior caval vein.

In Case 6 the highest catecholamine level was found in the left renal vein (Fig 1f) but the tumor was situated in the right adrenal. Low right renal vein concentrations indicate drainage from the tumor into the right renal vein to be unlikely, thus, jetting of blood from the right side as a contaminant to the left would not be expected. An aortography and a selective right renal epinephrine angiography demonstrated tumor on the right and following removal of this the patient remained normotensive for three years with normal urinary VMA. At four years control a slightly elevated VMA was found (8.4 mg/24 h) but the patient was still free of symptoms and no further evaluation was made. Thus the possibility of a small pheochromocytoma on the left side exists. Such errors may be minimized by samples from veins in immediate proximity to the expected tumor site such as the adrenal veins (Cases 5 and 7, Fig 1c, g).

Our limited experience with alpha and beta receptor blocking agents do not allow a conclusion as to the extent these agents interfere with measurements of pressor substances. (Two facets are involved here: both pressor substance production—release and actual measure thereof. Assuming a nonbiologic in vitro measuring system, at least measurement of catecholamines should theoretically be unaffected.) In Cases 5 and 7 high catecholamine values were found in spite of administration of dibenzylline the day before and during examination. Hence it is also reasonable to assume as theoretically expected that the hormonal activity and pressor substance release are not influenced by alpha receptor blocking agents. In addition, dibenzylline administered before angiography did not prevent a vasoconstrictive response to intraarterially injected epinephrine in a dose of 6 to 8 μ g (contrary to what one might anticipate, probably dose related). In spite of premedication with blocking agents one hypertensive crisis ensued following adrenal phlebography but did not require

FIG. 6. Case 3. a) Aortography. Tumor in the left adrenal gland (\rightarrow) left in situ 1 year after nephrectomy 6 1/2 years earlier. Left renal artery is located; the details of the vascular supply and drainage are uncertain. b) Celiac angiography following intraarterial injection of 8 μ g epinephrine. Multiple small branches of the splenic artery feeding the tumor. c) Venous phase. The tumor is more clearly defined but the precise routes of its venous drainage are not defined. Central venous catecholamine assay (Fig 1) strongly indicates anomalous drainage into the inferior caval vein subsequent to the previous surgery.

treatment with phentolamine. This event emphasizes the desirability of premedication with blocking agents for adrenal phlebography as well as angiography corroborating an observation of GOLD et coll. (1972).

Because the angiographic search for a pheochromocytoma may require examination of several vascular beds and be quite time consuming with resultant higher risks to the patient, it would be ideal that venous catheterization and adrenal phlebography be performed before angiography. With such information available, the angiographic effort might be focused to a particular level and side with deletion of unnecessary selective arterial examinations. Logistic and economic considerations may prevent the ideal sequence, however, and Cases 6 to 8 were examined with at least 2 methods in the same session. The total examination time in these did not exceed 2 hours and maximum diagnostic information for localization of the pheochromocytoma was obtained.

Acknowledgements

The authors are indebted to Dr Nils Juel Christensen, Aarhus Kommunehospital, Denmark for catecholamine determinations in Case 8 and Dr John M. Reed, Baptist Memorial Hospital, Jacksonville, Florida for data on Case 9. Mr Robert Beach, medical illustrator at the University of Florida, did the basic art work in Figure 1.

SUMMARY

Preoperative diagnosis and localization of pheochromocytoma in 10 patients (13 tumors) by aortography, selective angiography, adrenal phlebography and catecholamine measurements in central veins are discussed. While there are pitfalls, the combined use of these methods resulted in a diagnosis of all tumors preoperatively. Alpha receptor blocking agents to prevent or reduce hypertensive crises should be given not only before angiography but, before venous catheterization, particularly when phlebography is anticipated.

ZUSAMMENFASSUNG

Die präoperative Diagnose und Lokalisation von Pheochromozytomen bei 10 Patienten (13 Tumoren) durch Aortographie, selektive Angiographie, Nebennierenphlebographie und Catecholamin-Messungen in den zentralen Venen werden diskutiert. Obwohl Fallstricke vorhanden sind, ermöglicht die kombinierte Verwendung dieser Methoden eine präoperative Diagnose aller Tumoren. Alpha-rezeptor blockierende Substanzen sollten nicht nur vor der Angiographie gegeben werden, um hypertensive Krisen zu vermeiden, oder zu verringern, sondern auch vor der Venenkatheterisierung, besonders wenn eine Nebennierenphlebographie beabsichtigt ist.

RÉSUMÉ

Les auteurs examinent des diagnostics préopératoires et la localisation de phéochromocytomes chez 10 malades (13 tumeurs) par aortographie, angiographie sélective, phlébographie surrénalienne et dosage des catécholamines dans les veines centrales. Bien que ces méthodes présentent des causes d'erreur, l'utilisation combinée de ces méthodes a abouti

un diagnostic préopératoire de toutes les tumeurs. Les agents bloquant les alpha récepteurs pour prévenir ou pour réduire les crises hypertensives devraient être administrés non seulement avant l'angiographie mais aussi avant le cathétérisme veineux, particulièrement quand on prévoit de faire une phlébographie surrénalienne.

REFERENCES

- BORGES E, WILLIAMS C M and JUDSON M P. Angiography of pheochromocytoma. *Amer J Roentgenol* 96 (1966) 225.
- BURGER W, GRIMMEL H and SIKEMER H. Zur Lokalisation des Phäochromocytoms. *Med Klin* 61 (1966) 533.
- BUSH J E and MAHER V B. Adrenox cortical hyperfunction with sudden onset of hirsutism. *J Endocr* 18 (1959) 1.
- CLARKEON cited by BUSH and MAHER.
- DIXE W W, BOSHELL, B R, SOTERIS P and CARR J H Jr. A norepinephrine secreting glomus jugulare tumor presenting as pheochromocytoma. *Ann intern Med* 60 (1964) 1040.
- ELLER U S, GEMZELL C A, STROM G and WESTMAN A. Report of a case of pheochromocytoma with special regard to preoperative diagnostic problems. *Acta med scand* 153 (1955) 127.
- GOLD R E, WEINGER B M, GERACI A R and HENRI L M. Hypertensive crisis as a result of adrenal venography in a patient with pheochromocytoma. *Radiology* 102 (1972) 579.
- GRIM C E, OLSON J F, WYNN J O and CAULIN CLAVELLA J Jr. Bilateral pheochromocytoma. The application of plasma catecholamine bioassay for tumor localization. *Amer Heart J* 74 (1967) 809.
- HARRISON T S, BARTLETT J D Jr and SEATON J F. Current evaluation and management of pheochromocytoma. *Ann Surg* 168 (1968) 701.
- JONSTON F R O. The suprarenal veins. *Amer J Surg* 94 (1957) 615.
- KARY P O and NIKROZ L V. Selective angiography of the adrenal glands. *Amer J Roentgenol* 101 (1967) 739.
- KAUTZ J V and ADGE O F. Angiographic diagnosis of pheochromocytoma. *J Amer med Ass* 207 (1969) 1333.
- LANIER L O and ROSENCRANTZ M. Arteriographic appearances of pheochromocytoma. *Acta radiol Diagnost* 10 (1970) 35.
- MENCHER W H. Perirenal insufflation. *J Amer med Ass* 109 (1937) 1538.
- MIKHELEVICH C G. Epinephro-phlebography of benign tumours. *Acta radiol Diagnost* 8 (1969) 129.
- REUTER S R, BLAIR A J, SCHETTERDART D E and BOOKSTEIN J J. Adrenal venography. *Radiology* 89 (1967) 803.

- SAPPA J. D., ALANIECKI T. and RATKIN G.: Von pheochromocytoma. *J. Amer. med. Ass.* 212 (1970) 2243.
- SCHMID E. und KRAUTHIERM J.: Diagnostische Suchmethoden bei hormonal aktiven Sympathikus-tumoren. *Med. Welt (Berl.)* 20 (1969) 859.
- SIEGEL S. G.: Current experience in the diagnosis of pheochromocytoma. *Circulation* 34 (1966), 473.
- SUTTON D.: Diagnosis of Conn's and other adrenal tumors by left adrenal phlebography. *Lancet* I (1968) 453.
- TELENITS M., LUNDEGOTT A. and CHRISTENSEN N. J.: Diagnosing pheochromocytoma by selective suprarenal angiography and a new enzymatic catecholamine assay. To be published in *Acta endocr. (Abh.)*
- WILLIAMS C. M. and GREER M.: Gas chromatography of urinary anilmandelic acid in pheochromocytoma. *Clin. Chim. Acta* 11 (1965) 495.

ANGIOMYOLIPOMA (HAMARTOMA) OF THE KIDNEY

An angiographic review

J A BECKER M KINKHABWALA H POLLACK and M BOSNIAK

The angiomyolipoma or hamartoma is an uncommon lesion of the kidney that is infrequently diagnosed before histologic examination. The roentgen observations suggesting this diagnosis at urography and angiography have been previously reported but usually with only a single case or so in illustration. The purpose of this communication is to review the angiographic findings of these case reports and to add 18 previously unreported cases all examined by angiography. Reports with incompletely examined cases were excluded from this review.

Discussion and observations

Hamartomas of the kidney are commonly divided into two groups: those appearing as multiple lesions of the kidneys, commonly with tuberous sclerosis and those appearing as solitary lesions, usually unassociated with any syndrome. Sixty to eighty per cent of patients with tuberous sclerosis will have multiple renal lesions (LADO & GONZALEZ 1967; MARSHALL et al 1959) and with the full

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Fig. 1 (a) The arterial phase demonstrates a circumferential group of vessels delineating the lesions with whorled or sunburst appearance on the capillary nephrographic phase (b). This appearance is seen throughout the majority of lesions within both kidneys.

clinical stigmata of tuberous sclerosis, with the urography simulating adult polycystic disease, and with the angiographic appearance similar to carcinoma of the kidney, the clinical roentgen diagnosis is usually straightforward. However, when a solitary lesion is present within the kidney and no systemic findings are present, the clear cell carcinoma is the prime angiographic suggestion rather than the hamartoma. Although a pre-operative diagnosis of hamartoma may be made, this may not preclude surgical intervention because of the possibility of these lesions to eventually produce symptoms. Also, the angiographic examination, whether diagnostic for a hamartoma or not, will influence the surgical approach and, thus, is proper in the evaluation of any renal mass.

Age and sex. The ages of patients with a solitary lesion varied between 21 and 72 with an average of 48. In the solitary lesion, there was a predominance towards the female with a 23 to 4 ratio. The patients with tuberous sclerosis tend to be younger with a range of 11 to 41, an average age of 30.6. In this



Fig 2 The angiographic examination demonstrates less prominent ascularization but an appearance of small to large aneurysm formation. This is an unusual appearance for clear cell carcinoma and is more typical for the hamartoma. (Courtesy of Emmanuel Levin, Director of Radiology, Montefiore Hospital, Brooklyn, New York.)

group, there was also a sex predominance with 6 out of 7 patients female. These findings correlate well with those of McCULLOUGH et coll (1971) in their excellent and extensive review of this subject.

Urologic symptoms. The patients generally had vague urinary tract abdominal symptoms and the renal lesions were accidental findings in the course of a non-specific general examination. In the patients with tuberous sclerosis renal lesions were specifically sought despite the fact that they also had essentially no urologic symptoms. The most common presenting symptom was that of flank pain that may well be representative of renal capsular distension secondary to the mass lesion. Only 3 patients presented with gross hematuria, none of the incidents life threatening. This places hematuria in a minor aspect contrary to the report by KESSEL (1965) where massive hematuria was felt to be a significant sign. Three patients had localized hematomas but did not have hematuria. Thus it



b



Fig 3 a) Areas of calcification or resting fat (→) are seen within the mass on the initial film of the abdomen b) On the angiographic examination the lesions are non-descript and are felt to mainly represent findings associated with the least cell carcinoma. None of the suggestive signs that are felt to be associated with hamangioma are present



Fig 4 The renal mass lesion—non specific in angiographic appearance. A suprarenal mass avascular separates the kidney and adrenal. At surgery this represented an encapsulated hematoma.

must be assumed that spontaneous bleeding is not a common symptom or sign. Similar observations have been reported by Pizarro et coll (1960) and Vasko et coll (1965).

Tuberous sclerosis. Fourteen per cent of patients had overt clinical tuberous sclerosis as evidenced by adenoma sebaceum, mental retardation and roentgenologically the other classical findings of tuberous sclerosis. Two out of 7 patients with multiple lesions, however, did not have the classical clinical stigmata of this disease and this was felt to represent the gamut of presentations of tuberous sclerosis with the more minor presentations a form fruste of tuberous sclerosis.

Urography. On conventional films of the abdomen an area suggesting fat within the lesion was observed in only 9 per cent of patients even in retrospect. Calcifications associated with the mass were rare. Interstitial calcification was found in the lesion in 6 per cent of the cases. One patient had an amorphous calcification associated with the hamartoma and at pathologic examination this was considered as a benign calcification associated with the myomatous part of the tumor.

At urography the multiple lesions produced an appearance simulating adult polycystic kidney disease with the price taking areas within the kidney identical to that seen with multiple cysts. The solitary lesions, as would be expected, demonstrated a mass effect with no suggestion of a specific cause. In each of these instances the interpretation was that of a mass lesion of the kidney with a cyst or tumor the diagnostic possibilities. Further examinations such as nephrotomography and sonography confirmed the lesions as a solid mass and excluded a cyst.

The single striking factor in patients with unilateral disease was a marked predominance of the right kidney over the left. The lesion was located on the right side in 20 out of 27 patients.

Angiography Last reference has been made to the typical appearance of hamartomas (KILIANI et coll 1968; VIANOVY et coll 1966). Thirteen out of 27 solitary lesions and 5 out of 7 multiple lesions presented with the findings that the authors considered suggestive of hamartomas: circumferential peripheral vessels, sunburst or whorled appearance in the nephrographic phase (Fig 1) or multiple aneurysms (Fig 2). Aneurysmal dilatation were seen in 16 out of 34 cases, the most common of the angiographic findings. As with the whorled nephrogram this suggests hamartoma but has also been seen in clear cell carcinoma of the kidney. The appearance was no more common in tuberculous scleroses with diffuse lesions than in the individuals presenting with a solitary renal mass.

Histologic examination hopefully would have given an explanation to the angiographic appearances and indicated the prominent component producing the roentgen findings. However the microscopy commonly did not specify pre dominance of one of the mesenchymal elements over the other. Thus, this correlation could not be made based on the current material.

A significant angiographic observation was the absence of art. non. enous shunt early venous filling (major renal veins) was never seen. Arterio. nous puddling common in most profound neovascular processes was seen. In the two cases that were reported as angiosarcomas the angiographic findings were identical to those of the associated benign lesions. No evidence of renal vein involvement or distant metastases was seen. From the angiographic findings these malignant tumors appeared identical to their benign counterparts. The question of their actual malignant nature must be questioned because of the controversy over the microscopic criteria of benign versus malignant in the complex mesenchymal tumor (HARTVET & HALLERAKER 1960).

Upon the roentgen appearance, 22 out of 27 cases would easily be considered clear cell carcinoma in the solitary lesion and 2 out of 7 in the multiple lesions.

Thus angiography is not felt to be a definitive diagnostic procedure (Figs 3-4).

SILBERG & PETERSON (1971) and PALMISANO (1967) used epinephrine in the examination of hamartomas of the kidney but found this of no value for the differential diagnosis. As is wellknown at the current time the neovascular process deficient in smooth muscle in the walls of its smaller arteries does not respond to epinephrine at appropriate dose levels. Epinephrine has not been a help in the differentiation between newly formed vessels in benign, malignant or inflammatory lesions.

Of the roentgen methods available the diagnosis of fat within the lesion is felt to be the most secure finding for the diagnosis of hamartoma (ADELMAN 1965; GROSETT 1966).

SUMMARY

Thirty-four cases of hamartomas of the kidney have been reviewed. In some instances the appearance of fat on conventional films and circumferential arteries and veins with a sunburst or whorled appearance or multiple aneurysms at angiography suggest hamartoma but a clear cell carcinoma may produce similar finding. Where multiple lesions of the kidney are associated with tuberous sclerosis the diagnosis is usually obvious.

ZUSAMMENFASSUNG

Vierunddreissig Fälle eines Hamartoms der Niere werden zusammenfassend besprochen. In einigen Fällen lassen das Vorkommen von Fett auf konventionellen Bildern und von umgebenden Arterien und Venen mit einem sonnenstrahlenartigen oder kränzenartigen Bild oder multiplen Aneurysmen bei der Angiographie ein Hamartom vermuten. Unzweifelhaft Zellkarzinome können jedoch ähnliche Bilder hervorrufen. Wenn multiple Läsionen der Niere mit einer tuberösen Sklerose verbunden sind, ist die Diagnose gewöhnlich klar.

RÉSUMÉ

Trente quatre cas d'hamartome de rein ont été passés en revue. Dans certains cas l'image de tumeurs graisseuses sur les radiographies simples, la présence d'artères circonferentielles et de veines avec un aspect en rayons de soleil ou en tourbillon, ou des anévrismes multiples visibles sur l'angiographie font penser à un hamartome mais un cancer à cellules claires peut donner un aspect semblable. Quand il y a des lésions rénales multiples associées à une sclérose le diagnostic est habituellement évident.

REFERENCES

- ADELMAN, A. B. Angiomyolipoma of the kidney. *Amer. J. Roentgenol.* 95 (1965) 403.
 BRENDLER, H., MAOCHER, J., MITTY, H. Angiographic characteristics of renal hamartoma. *Brit. J. Urol.* 43 (1971) 674.
 CLARK, R. and PALMERONAS, A. The angiographic spectrum of renal hamartoma. *Amer. J. Roentgenol.* 114 (1972) 715.

- CROFTT A Roentgenographic findings in the renal lesion of tuberous sclerosis *Amer J Roentgenol* 98 (1966) 739
- FAKMEZ S JUNGHAUSEN P RAN O and SALTZMAN G F Hamartoma (liposarcoma) of the kidney *Acta radiol Diagnosi* 7 (1968) 417
- HARTVIT F and HALLEBRAKER D A report of three angiolipomyomas and one angio-myosarcoma *Acta path microbiol scand* 49 (1960) 329
- KRISHN J Three cases of renal hamartoma two cases presenting with spontaneous rupture and massive retroperitoneal hemorrhage *J Urol* 94 (1965) 336
- KHILNA I M ABRAHAM R and BERANBAUM E Angiographic features of hamartoma of the kidney A case report *Radiology* 90 (1968) 999
- LACOS J and GOSWZ M Tuberous sclerosis Reappraisal of a clinical entity *Mayo Clin Proc* 4 (1967) 26
- LOVE L and FRANK J Angiographic features of angiomylipoma of the kidney *Amer J Roentgenol* 95 (1965) 406
- MARSHALL D SAUL G and SACHS L Tuberous sclerosis A report of 16 cases in two family trees revealing genetic dominance *New Engl J Med* 261 (1959) 110
- McCOLLOUGH D SCOTT R and SEYBOLD H Renal angiomylipoma (hamartoma) Review of the literature and report of seven cases *J Urol* 105 (1971) 32
- PALMBANO P Renal hamartoma (angiomylipoma) *Radiology* 88 (1964) 49
- PEROL M and GRIVY P Mesenchymal hamartomas of the kidney *J Urol* 83 (1960) 40
- SEABURY J ENGBER R and WOLFE Q Angiomylipoma of the kidney A benign tumor demonstrating neo-vascularization by arteriography Report of cases *J Urol* 98 (1967) 562
- SILBERG M and PETERSON C Renal angiomylipoma Its distinctive angiographic characteristics *J Urol* 106 (1971) 363
- UDENVAL F Renal angiomylipoma Clinical and pathologic study I : *J Surg* 46 (1966) 705
- VAIKO J BROCKMAN S and BOWEN R Renal angiomylipoma A rare case of spontaneous massive retroperitoneal hemorrhage *Ann Surg* 161 (1965) 577
- VIAMONTE M RAHEL R POLITANO A and BRIDGES B Angiographic findings in a patient with tuberous sclerosis *Amer J Roentgenol* 98 (1966) 723

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THROMBOGENIC PROPERTIES OF HEPARINISED VASCULAR CATHETERS

B JACOBSSON and D SCHLOSSMAN

Methods for comparing the thrombogenic properties of catheter materials *in vitro* (JACOBSSON & SCHLOSSMAN 1973) and *in vivo* (SCHLOSSMAN 1973 a b) have previously been described. These methods make it possible not only to select the least thrombogenic material available but also objectively to evaluate any measures undertaken to reduce the defect. Though various procedures such as change in the surface charge, plasma protein coating and heparinisation (GOTT 1966, MURPHY *et al* 1967, SAWYER *et al* 1970) have been suggested for counteracting thrombus formation on foreign surfaces in the circulation, heparinisation is probably still the only one that may be applied to vascular catheters.

The present authors in the publications referred to stressed that the thrombogenic quality of a material should be judged from its tendency to initiate thrombus formation. It was also indicated that comparisons of the reaction of the platelets to the materials, i.e. platelet adhesion *in vitro* and the amount of platelets in thrombi on the materials *in vivo* respectively, are both simple and practical for this purpose.

The intention of the present investigation was to evaluate the antithrombogenic effect of heparinisation of catheter materials *in vitro* and *in vivo* as estimated with the methods mentioned.

Materials and Methods

Heparinisation The method used for heparinisation of the catheter compounds has been described in detail by LAGERGREN & FRIDSSON (1971) and consists of three main steps. The polymer surface is first covered with a layer of positively charged groups of ions by immersing it for 30 minutes in a circulating 1 mM solution of octadecyltrimethylammonium propylamine dihydrochloride (AB Kema, Stockholm) at a temperature of 85 °C. The surface is then thoroughly rinsed and cooled with distilled water. At the temperature mentioned the molecules of the cationic surfactant penetrate into the surface of the polymer so that when the latter is cooled the surfactant molecules are trapped in their positions to give the surface a layer of positive ionic groups.

The cationic surface of the polymer is then bound in a streaming solution of heparin (Heparin Vitrum) and 0.9% saline for 2 hours at a temperature of 75 °C. The concentration of heparin in the solution is 10 IU/ml and the pH is adjusted to 3.6 by the addition of hydrochloric acid. The polymer is then rinsed with distilled water. The resulting concentration of heparin on the surface of the polymer is 3 to 5 IU/cm². As this binding of heparin is unstable on exposure of the surface to blood, the polymer is finally immersed in 1% glutaraldehyde solution at 60 °C for 10 minutes. This third step results in cross-linkage of the heparin molecules with the formation of a heparin network ionically anchored to the polymer surface.

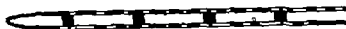
Experiments

Polyethylene (PL 260 Intramedic, Clay Adams) was the catheter compound investigated. When radioactive platelets were used the labelling was performed *in vitro* with ⁵¹Cr by the FOSS ABRAHAMSEN (1968) modification of the method of AAS & GARDNER (1958). The radioactivity was measured with a 7.6 cm NaI well crystal (Autowell III Picker).

Experiments *in vitro*

The method and set up for comparing platelet adhesion to different vascular catheter materials *in vitro* have been described in detail in a previous paper (JACOBSSON & SCHLOSSMAN). This method enables adhesion to be calculated from counting of human or dog platelets as well as from measurement of the radioactivity of labelled dog platelets.

The experiments were carried out in three series, viz. 5 dogs with labelled platelets (series I), 5 other dogs with unlabelled platelets (series II) and 5



Positions of pieces of catheter materials in control and test devices. In the control device all compartments consist of polyethylene and in the test device of polyethylene (left) heparinized and sterilized polyethylene (middle) and heparinized polyethylene (right)

human blood donors (series III). Venous blood in all the experiments was obtained in 10 ml aluminium glass tubes containing 1 ml of 3.8% trisodium citrate solution ($\text{Na}_3\text{C}_6\text{H}_5\text{O}_7 \times 2 \text{ H}_2\text{O}$). About 15 minutes later 1 ml of the citrated blood was transferred to each of three ordinary polyethylene catheters and three heparinized polyethylene catheters. The ends of each catheter were joined by a plastic outer muff and the catheters, all of which were 1 meter long, then rotated on a slanting turntable at room temperature for one hour. The blood in the catheters was then poured into separate tubes. The mean of the relative decreases in platelet concentrations in each set of three parallel determinations was taken as a measure of platelet adhesion.

The concentration of platelets in the blood samples in series I was calculated from the radioactivity of the sample—in series II and III from platelet counts. Every test was performed with blood from a new donor. The dog platelets were labelled 1 to 2 days before the experiments. The unlabelled platelets were counted with Björkman's (1959) method but without the use of EDTA.

Means of paired differences of observations were compared by Student's *t* test at the significance level of 0.05.

Experiments in vivo

The device. The device and principle used for comparing the thrombogenicity of vascular catheters of varying materials *in vivo* have been fully described previously (Schlossman 1973 a, b). The devices were made up of three pieces of catheters connected with wooden pins and provided with a standardised number of side holes. The pieces of equal length were intended for insertion into the aorta by transfemoral catheterisation; the side holes permitted the flow of blood through the pieces and thereby formation of thrombi on their inner surface. On withdrawal of the devices thrombi adhering to the pieces of materials were thus readily available for analysis.

The experiments to be described concern two kinds of devices used alternately and will be referred to as control devices and test devices. The former were made up of pieces of untreated polyethylene only, while the test devices consisted of untreated polyethylene, heparinized polyethylene and polyethylene

Table 1

Adhesion (per cent) of platelets to vascular catheter materials in vitro. Mean values of five experiments

	⁵¹ Cr dog platelets	Dog platelets	Human platelets
Polyethylene	23	32	34
Heparinized polyethylene	0	13	1

sterilised after the heparinisation. The positions of the pieces of the material in the control and test devices appear in the figure. Sterilisation of the compounds was performed by gamma radiation with 3.2 Mrad (AB Radona, Skärhamn, Sweden).

Procedure The platelets of 2 mongrel dogs weighing 18 and 22 kg were labelled the day before the experiments; the latter were performed under light anaesthesia induced and maintained by repeated small intravenous doses of thionembutal sodium (Pentothalodium, Abbott). The animals were in the fasting state, placed on a warm table and during the experiments given isotonic saline intravenously at a rate of approximately 2 ml/kg body weight.

Six test devices and six control devices were placed alternately in the aorta of each dog. The devices were withdrawn after 5 minutes exposure to the blood stream and the amounts of thrombi on the pieces of material estimated from their content of ⁵¹Cr labelled platelets.

Calculation and statistical analysis For each test device the thrombi formed on untreated polyethylene were used as references in the calculation of the amounts on the pieces of heparinized and heparinized as well as sterilized, polyethylene. The activity on the pieces of each control device was likewise calculated relative to that on the piece of polyethylene in the same position as the pieces of polyethylene in the test devices. Differences between the identical pieces in the control device were attributed to sources of variation not ascribable to variations between the materials. The former differences will hereinafter be referred to as the error of the method. By comparing the differences between untreated polyethylene and any other piece in the test devices with those between two pieces of untreated polyethylene in corresponding positions in the control devices in each animal, it was possible to determine whether the variations between the different kinds of polyethylene were significant. The calculations were made with the Wilcoxon test at a significance level of less than 0.05.

Table 2

Thrombogenic properties of vascular catheter materials in vivo. Mean values of six experiments on each of two (= A and B) devices for non-heparinised catheters in corresponding portions in control and test devices were said to be 100

	Control			Test		
	Polyethylene	Polyethylene	Polyethylene	Polyethylene	Heparinised and sterilised polyethylene	Heparinised polyethylene
A	100	108	99	100	31	35
B	100	113	104	100	40	40

Results

Heparinisation resulted in a significant reduction in the thrombogenic property of the catheter material both in vitro and in vivo. Heparinisation in the in vitro experiments thus reduced the adhesion of platelets to the material whether adhesion was calculated from the ^{51}Cr activity or platelet counts (Table 1). No qualitative difference was evident between the reaction of the human and dog platelets.

In the in vivo tests heparinisation caused a larger reduction in the ^{51}Cr activity on the materials than could be explained by the error of the method. The effect of the heparinisation was not affected by sterilisation with gamma radiation (Table 2).

Discussion

The findings indicated that heparinisation reduces the thrombogenicity of catheters, as judged from the criteria employed. The agreement between results of the tests in vitro and in vivo, the former including also human blood, suggests that the effect of heparinisation holds also for the human circulation.

Sterilisation by gamma radiation proved to have no influence on the heparinisation—an observation of considerable practical importance.

The first method for heparinisation was described by Gott et al. (1967) since when several others have been devised (Eriksson et al. 1967, et coll. 1967; Lagergren et coll. 1968; Groner et coll. 1969; Mörner et al. 1970). These have made it possible to heparinise a wider variety of materials and to attach the heparin in different ways. Judging from the literature, the stability of the heparin linkage and thereby the effect of the catheter on contact with blood or plasma may vary with the method used.

10. LAERGERGREN & ERIKSSON their method results in a stable linkage of the heparin, thanks, above all to the cross-binding with glutaraldehyde.

Previous evaluations of heparinised materials *in vitro* have reflected mainly the delayed clotting on the surfaces and *in vivo* mainly the extended patency of shunts and tubes in the circulation (GOTT LEININGER *et coll* 1966 GRODE *et coll*).

Remarkably few investigations have been published on the interaction between platelets and heparinised surfaces. LEININGER *et coll* have however reported in a preliminary communication that heparinisation of a surface reduces the adhesion of platelets, an observation corroborated by the present investigation. SALZMAN *et coll* (1969) on the other hand, found an increased deposition of platelets on heparinised materials *in vitro*; their results are not however comparable with those now reported for they used a different type of heparinised material and a different test method. Furthermore they did not describe the method of heparinisation applied and failed to confirm the deposition of platelets on the material *in vivo*. An increased adhesion of platelets to heparinised surfaces may be explained by incompleteness of the heparin coating of the surface (GRODE *et coll*). With an incomplete coating negatively charged platelets will be exposed to positively charged surfactants and consequently increased platelet adhesion is apt to occur.

Thrombus formation on heparinised vascular catheters has been previously investigated in animals by GLANCY *et coll* (1970) and AMPLATZ (1971). The former based their results on findings at autopsy, the latter at angiography. Both investigations indicated decreased thrombus formation on the heparinised materials. GLANCY's investigation included catheters heparinised by the method of ERIKSSON & LAERGERGREN.

The value of heparinisation with permanent implants such as artificial heart valves and vessel grafts depends essentially on the expected duration of the antithrombogenic effect. The results of longterm investigations have suggested that the effect lasts for at least weeks though longer effects are less well documented. However in vascular catheterisation, which is usually of short duration even the delay of thrombus formation is of much clinical value. Moreover the necessity of keeping the surfaces clean, i.e. free from thrombi is perhaps still greater with catheters than with permanent implants. An angiographic catheter for example must be withdrawn through the puncture so that thrombotic deposits may be wiped off with consequent risk of thromboembolism.

Sampling of blood as well as infusions through catheters is not infrequently rendered impossible by clotting of blood in the catheter. The known prolongation of the clotting time of blood on heparinised surfaces is therefore an additional advantage of heparinised catheters.

Though many investigators (WHITTEN et coll 1964 GOTT SALZMAN et coll) have tried to explain the mode of action of the anti thrombogenic effect of heparinisation of materials the mechanism is still obscure. Since heparin is however a substance normally occurring in the body the absence of knowledge of its mode of action should not preclude the utilization of its desirable properties. A clinical trial with heparinised catheters is therefore obviously reasonable.

SUMMARY

The thrombogenic properties of the heparinised polyethylene catheters was compared with those of untreated polyethylene in *in vivo* in dogs and *in vitro* in dogs as well as in human subjects and the platelet reaction to the materials taken as a measure of the defect. Heparinisation always resulted in significant decrease in the thrombogenic power of the materials.

ZUSAMMENFASSUNG

Die Thrombose hervorrufenden Eigenschaften heparinisierter Polyäthylenkatheter wurden *in vivo* an Hunden und *in vitro* an Menschen mit denen von unbehandelten Kathetern verglichen. Dabei wurde die Thrombozytenreaktion als Mass der Schädigung verwendet. Heparinisierung führte stets zu einem signifikanten Abfall der Thrombose hervorrufenden Eigenschaft des erschudenen Materials.

RÉSUMÉ

Les auteurs ont comparé les propriétés thrombogéniques des catheters en polyéthylène heparinisés avec celles du polyéthylène non traité *in vivo* chez des chiens et *in vitro* chez des chiens ainsi que chez des sujets humains et ont pris la réaction plaquettaire ces matériaux comme mesure de cette propriété. L'heparinisation a toujours entraîné une diminution significative du pouvoir thrombogénique de ces matériaux.

REFERENCES

- VALE A. and QUADDER F. H. Survival of blood platelets labelled with chromium 51. *J. clin. Invest.* 37 (1958) 1207.
 AMPLATE A. A simple non thrombogenic coating. *Invent. Radiol.* 6 (1971) 780.
 BJORKMAN S. E. A new method for enumeration of platelets. *Acta haemat. (Basel)* 22 (1959) 577.
 ERDMAN J. C., GULLBERG G. and LAGERGREN H. A new method for preparing nonthrombogenic plastic surfaces. *J. Biomed. Mater. Res.* 1 (1967) 301.
 FOW ABRAHAMSEN A. A modification of the technique for ⁵¹Cr labelling of blood platelets giving increased circulating platelet radioactivity. *Scand. J. Haematol.* 5 (1968) 53.
 GLANCY J. J., FREEMAN G. and HENDER E. R. Nonthrombogenic arterial catheters. *Amer. J. Roentgenol.* 108 (1970) 716.
 GOTT V. L. The causes and prevention of thrombosis on prosthetic materials. *J. surg. Res.* 6 (1966) 274.
 — WHITTEN J. D. and DUTTON R. C. Heparin bonding on colloidal graphite surfaces. *Science* 142 (1963) 1297.

- GRODE G A ANDERSON S J GROTTA H M and FALB R D Nonthrombogenic materials via a simple coating process Trans Amer Soc artif intern Organs 15 (1969) 1
- JACOBSSON B and SCHLOSSMAN D Thrombogenic properties of vascular catheter materials *in vivo* Acta radiol Diagnosis 14 (1973) 385
- LACROIX H FORBES N FRIEDMAN J C and GILBERT G Preparation and evaluation of nonthrombogenic surfaces J thorac cardiovascular Surg 56 (1968) 381
- and FRIEDMAN J C Elastics with a stable surface monolayer of cross linked heparin preparation and evaluation Trans Amer Soc artif intern Organs 17 (1971) 10
- LEVINOFF R I EPSTEIN M M FALB R D and GRODE G A Preparation of nonthrombogenic plastic surfaces Trans Amer Soc artif intern Organs 12 (1966) 151
- MERRILL E W SALZMAN E W WONG P S L ASHFORD T P BROWN A H and AUSTIN W G Polyvinyl alcohol heparin hydrogel G J appl Physiol 29 (1970) 723
- MURPHY P HOLLY I VAN SOMEREN L BANKOLE M SINGH S and BERNARD W F Antithrombogenic properties of electrified polymers Trans Amer Soc artif intern Organs 13 (1967) 131
- SALEM M E W AUSTIN W G LIPPES B J MERRILL E W GILLILAND R R and JONES J A new antithrombotic surface Development and *in vitro* and *in vivo* characteristics Surger 61 (1967) 1
- MERRILL E W BINDER A WOLF C F W and ASHFORD T P Protein platelet interaction on heparinized surfaces J Biomed Mater Res 3 (1969) 69
- SAWYER P N S KINTANUS S CHOPRA I S MARTIN J G LUCAS T BRIDGEMAN C B and SAUVAGE L Electrochemistry of thrombosis—An aid in the selection of prosthetic materials J Biomed Mater Res 4 (1970) 43
- SCHLOSSMAN D (a) Thrombogenic properties of vascular catheter materials *in vivo* A device and objective method for comparing thrombus formation on vascular catheter materials Acta radiol Diagnosis 14 (1973) 97
- (b) Thrombogenic properties of vascular catheter materials *in vivo* Demonstration of differences between materials Acta radiol Diagnosis 14 (1973) 186
- WHITTEN J D YOUNG W P and GOTT V L Stability of the thrombus resistant graphite benzalkonium heparin surface in an anti heparin environment J thorac cardiovascular Surg 48 (1964) 317

VASCULAR COMPLICATIONS FOLLOWING NEEDLE PUNCTURE OF THE LIVER

An angiographic investigation in the rabbit

CH. HELLEKANT and T. OLIN

Needle biopsy and transhepatic cannulation of blood vessels and bile ducts of the liver have been used for several years. Owing to the proximity of the systems short circuits may sometimes occur after puncture. It was therefore thought worthwhile to investigate experimentally possible vascular complications following the procedure.

Material and Methods Twenty-eight Swedish land rabbits weighing between 1.4 and 3.4 kg were anaesthetized with pentobarbitone sodium intravenously. A catheter (OPP 60 OD/ID 1.15/0.75 mm) with a long tapered tip bent about 30° was introduced into the common hepatic artery through one of the femoral arteries under magnification fluoroscopy. Twofold (0.3 mm focal spot) or fourfold (0.1 focal spot) magnification angiography was performed with a film changer (AOT 24 cm × 30 cm) and high pressure injector 2 to 3 ml I opaque Cerebral (meglumine metrizoate) being injected at a rate of about 0.5 ml/s. Technical data: 90 kV 3.2 mAs 0.032 s—twofold magnification and 90 kV 1.6 mAs and 0.03 s—fourfold magnification. RP film and Rubin screens. Film programme 6/3 4/8 films/s.

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Fig. 1. Hepatic arteriogram after needle puncture. Lateral projection. Extravasation in the central part of the liver.



Table 1

Angiographic findings immediately after needle biopsy of the liver in 8 rabbits

	N. of animals
Arteriovenous shunt	7
Extravasation	9
False aneurysm	2
Increased circulation in punctured area	1
Normal	14

Table 2

Angiographic findings immediately after biopsy and one week later in 17 animals

	Immediately after (case No.)	Total	One week later (case No.)	Total
Arteriovenous shunt	5 6 10 16	4	2 5 6 10 1 19	8
Extravasation	6 9 12 19 20	5	—	1
False aneurysm	17	1	17	1
Normal	2 8 13 14 15	5	8 9 13 14 1 16 20	7

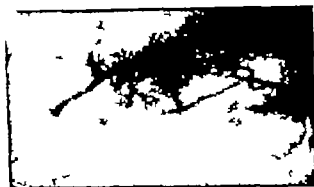


Fig 2 Hepatic angiography one week after needle puncture. Large arterioportal shunt (→)

The abdomen was opened following preliminary angiography by a high midline incision and the liver punctured from one entrance hole in three directions under direct visual control with a cannula OD/ID 0.9/0.55 mm. Control angiography was then performed and if the animal was to survive the abdomen was closed. Half of the rabbits were killed immediately after the control angiography and further angiography was carried out a week later in the other half. A total of 20 rabbits were also subjected post mortem to barium angiography.

Results

Vascular complications were encountered in 14 of 28 rabbits immediately after the biopsy (Table 1). Arteriovenous shunts were revealed in 7 cases, always arterioportal. Extravasation of contrast medium was encountered in 9 cases (Fig 1), false aneurysms in 2, and increased circulation in the vicinity of the puncture in one case. Fourteen of the cases were considered normal. No spasm of the arterial ramification was evident after puncture.

Arterioportal shunts were present at the control at one week in 6 of 13 animals (Fig 2). No extravasation of contrast medium was seen but one false aneurysm was found (Fig 3). A comparison of the angiographic findings immediately after the puncture and at one week appears in Table 2. Two of the fistulas had closed during the week but one of the rabbits previously considered normal had a shunt. No extravasations were seen at the one week control but two of them instead occurred as shunts; the false aneurysm was unchanged. The barium angiographies post mortem verified the findings but failed to give any further information.

Two of the rabbits with normal angiography in this experimental material died, one and six days after the puncture, respectively. The latter had a small



Fig. 3 Post mortem hepatic angiography one week after needle puncture. False aneurysm centrally in the liver (\rightarrow).

infarction just beneath the liver surface but no other changes were found. Two of the animals with arteriovenous shunts died due to technical failures.

Discussion

Liver biopsy has been widely undertaken in the clinic for a long time and only a few complications have been encountered. LINDNER (1967) examined the data of 79 381 liver needle biopsies performed according to MENON (1958). The mortality in this material was 0.015 per cent and the other serious complications occurred in 0.34 per cent. Concerning vascular complications, bleeding was noted in 57 cases, 7 of those being fatal. LINDQUIST (1971) performed 2 611 liver biopsies and recorded severe haemorrhage in only one. The frequency of vascular sequelae in the present material is high. The differences between the clinical and experimental materials may have been due to varying efforts to discover vascular complications, different calibre of the biopsy needles and variations in species. Often no efforts were made to diagnose minor vascular abnormalities in the clinical material but active search with fourfold magnification angiography was performed *in vivo* as well as post mortem in the experimental material. With conventional clinical methods, vascular complications probably would not have been diagnosed so frequently. The biopsy needle used for the rabbits (OD/ID 0.9/0.55 mm) was of about the same calibre as the one used in human subjects although the calibre of the latter depends upon the purpose of the puncture. A fine cannula is usual for biopsy but for transhepatic cholangiography or splenoportal phlebography a much cruder system is applied with a nylon/teflon (1.45/1.0 mm) or polyethylene (2.2/1.1 mm) tube outside the cannula of stainless steel. A higher amount of vascular complications may be expected with such a crude puncture technique (MENON 1970). The puncture did not produce spasm of the hepatic arteries not conforming to findings for

example at renal biopsy (FAELUND *et coll* 1972). The species differences are hard to get around, some exist although the general construction of the liver in man and rabbit is similar (BLOCH 1955, RAPPAPOORT 1958). The fate of the different vascular complications is not clear from the short observation period. Extravasations disappeared or changed to an arteriovenous fistula, though rarely. Some of the arteriovenous shunts closed during the observation week. In the kidney the fibrinolytic of the urine will support the development or maintenance of shunts. In the healthy liver the concentration of fibrinolytic is low but in the cirrhotic liver it may be high (ASTRUP 1966). Treatment with fibrinolytic blockers as tranexamic acid will therefore affect shunts only in the latter. Other factors may however be of importance. Many patients subjected to hepatic puncture may have some condition with a faulty coagulation mechanism, e.g. vitamin K deficiency, low prothrombin and fibrinogen concentration in the blood. A control of the clotting mechanism before liver biopsy has been recommended (LINDNER 1967, LUNDQUIST 1970). The angioarchitecture of the liver is often much changed at liver disease, e.g. wide and irregular vessels at cirrhosis and carcinoma; this will also increase the risk of vascular damage at needle puncture. A complication feared has been bleeding into the peritoneal cavity; this investigation has suggested that other vascular complications are probably much more common. The effect on the general circulation of the arteriovenous shunts is certainly small due to the filtering effect of the liver (FOLLEY *et coll* 1971). However, arteriovenous shunts have a tendency to increase in size with time. If an arterioportal shunt becomes large enough the portal pressure will increase, cirrhosis may develop and gastrointestinal bleeding from the bile ducts or from oesophageal varices may occur (SCHILLING & McKEE 1953, TREDE *et coll* 1969). A false aneurysm may heal or enlarge. If it increases sufficiently in size it may rupture, e.g. into the portal vein and create an arteriovenous fistula or into a bile duct and cause hemobilia (FOSTER & SANDBLOM 1961). The reason why all the arteriovenous shunts of the present material have been of arterioportal type is unclear; explanatory factors could be that the portal ramifications are larger and wider than the branches of the hepatic vein system or differences in the composition of the blood in the two systems. The differences in the pressures in the portal and hepatic veins are probably of no importance. However, arterioportal shunts in clinical material are also much more common than arteriovenous shunts (FOLLEY *et coll* 1971, TREDE *et coll* 1969).

SUMMARY

Complications arising from needle puncture of the liver were investigated by angiography in an experimental material of 28 rabbits. Vascular injury could frequently be demonstrated. The immediate importance was slight but such lesions may increase and cause symptoms.

ZUSAMMENFASSUNG

Die Komplikationen im Zusammenhang mit der Nadelpunktion der Leber wurden angiographisch an einem experimentellen Material von 28 Kaninchen untersucht. Ein arterieller Schaden konnte häufig nachgewiesen werden. Die unmittelbare Bedeutung ist geringfügig, derartige Schädigungen können sich jedoch steigern und Symptome verursachen.

RESUME

Les auteurs ont étudié par angiographie sur un matériel d'expérience de 28 lapins les complications dues à la ponction hépatique à l'aiguille. Ils ont souvent pu mettre en évidence des lésions artérielles. Leur importance immédiate est petite, mais elles peuvent croître ou augmenter les symptômes.

REFERENCES

- ASTUMI T. Tissue activators of plasminogen. *Fed Proc* 25 (1966) 42.
- BLOCH E. H. The in vivo microscopic vascular anatomy and physiology of the liver as determined with the quartz rod method of transillumination. *Angiology* 16 (1965) 340.
- ERLUND L., GOTTILF J. and OLIN T. Arteriovenous fistulae in rabbit kidney studied by dilution technique and by angiography. *Scand J Urol Nephrol* 6 (1972) 84.
- FOLLEY W. J., TURCOTTE J. G., HOSKINS PR. A., BREA T. R. L. and ALLEN P. G. Intrahepatic AV fistulas between the hepatic artery and portal vein. *Ann Surg* 174 (1971) 849.
- FOSTER J. H. and SAMDALOW I. Portal hypertension secondary to hepato-portal arteriovenous fistula. *Ann Surg* 154 (1961) 500.
- LINDER H. Grenzen und Gefahren der perkutanen Leberbiopsie mit der Menghini-Nadel. *Dtsch med Wochschr* 9 (1967) 1751.
- LANDQUEST A. Liver biopsy with a needle of 0.7 mm outer diameter. *Acta med scand* 188 (1970) 473.
- Fine needle aspiration biopsy of the liver. *Acta med scand* (1971) Suppl. No 540.
- MENGOINI G. One second needle biopsy of the liver. *Gastroenterology* 33 (1958) 190.
- One second biopsy of the liver. Problem of its clinical application. *New Engl J Med* 283 (1970) 582.
- RAPPAPORT A. M. The architectural organization of the liver: relation to the reference base for liver function. *In* Liver function. Edited by R. W. Brauer. Vol. 4. Amer Inst Biol Science Washington D.C. 1958.
- SCHILLING J. A. and MOHRER F. W. Late follow up on experimental hepatic portal arteriovenous fistulae. *Surg Forum* 4 (1953) 392.
- THEDE M., LINDER F. and VOLLMER J. Arteriovenous fistula of the portal system. *J cardio-vasc Surg* 10 (1969) 254.

PROSTAGLANDIN E (PGE_1) IN PERIPHERAL ARTERIOGRAPHIES

L. A. CARLSON, M. ERICSSON and U. FRILSON

The blood flow at the time of injection of contrast medium is important in peripheral arteriography especially in investigations of the extremities. At a low flow rate diagnostic amounts of contrast medium may not reach the peripheral arterial branches. On the other hand a high blood flow with consequent dilution of the contrast medium may also lead to poor peripheral filling. It would appear that a flow of about 7 to 8 ml per 100 ml tissue and minute in a leg produces optimal contrast filling (ERICSSON 1965). Different methods have been employed to increase the blood flow in connection with peripheral arteriography, i.e. arterial occlusion and physical exercise, increase in the temperature of the extremities and vasodilators. Prascoline was used by WICKBOM & BARTLEY (1957). Hydergine has been recommended but has little effect (ERICSSON 1970). Bradykinin, histamine and acetylcholine have also been tried (ERICSSON 1965). Bradykinin seems to be the most useful of these physiologically occurring vasodilators for it is easy to handle and increases the blood flow to a sufficient level, no side effects have been reported. It must be continuously infused for 5 to 10 minutes and its effect is not sufficiently long lasting to allow repeat arteriography with one injection.



Fig. 1. Arteriography in a 52-year-old man. (a) Optimal filling of peripheral arteries before (a) and after (b) reduction of PGI_1 .

Prostaglandin I_2 (PGI_2), a member of the prostaglandin family, is a potent vasodilator (for review, see BERGSTROM *et al.* 1968). The slow intravenous injection of PGI_2 in man decreased the peripheral resistance (CARLSON *et al.* 1969) and its introduction into the brachial artery in as small a dose as 10^{-5} $\mu\text{g/kg}$ body weight/min increased the forearm blood flow (BRVICAUD & ORO 1969). This effect of PGI_2 on the peripheral blood flow indicated that its vasodilator effect would be useful for peripheral arteriography; a few cases in which it has been used are now presented.

Material and Method. Five men aged 52 to 63 and one woman aged 53 with symptoms of intermittent claudication were investigated. All patients except one 52-year-old man had arteriosclerotic changes in the legs; they had no other diseases. A grey Ödman—Ledin catheter was introduced through the right groin into the aorta, where the contrast medium was injected for the arteriography. When the effect of PGI_2 was to be tested the catheters were placed in the external iliac artery. In five patients Angiografin was used as contrast medium and in one case a new synthesized dimer Rayodal. The calves were investigated

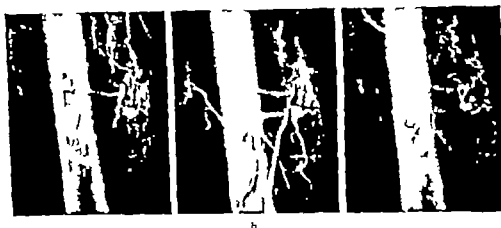


Fig. 3. Arteriography of the b of 55-year-old man with arteriosclerotic occlusion of the superficial femoral artery with collaterals. a) Without drugs. b) After beginning of injection of contrast medium. c) After injection of bradykinin. d) Following injection of contrast medium. e) After injection of PGE₁. f) After injection of contrast medium. The vasodilators bradykinin and prostaglandin shortened the transport time of contrast medium by two seconds and increased the number of visible small arteries.

in 2 cases and the thighs in 4 cases. First arteriography was performed with only contrast medium and after 15 minutes PGE₁ was slowly injected through the catheter into the external iliac artery. The solution was freshly prepared from a frozen sterile solution of PGE₁. The infusate had a concentration of 0.5 µg/ml PGE₁ and was administered at 0.7 µg/min over 10 minutes corresponding roughly to 10 µg/kg body weight/min. Immediately after this injection the

Table
Arteriographic effect of PGE₁ and bradykinin

Effects of PGE					Effects of Bradykinin				
Part examined	N	Reduction of transport time (seconds)	Improved filling of small arteries	Increase in diameters main artery collaterals	N	Reduction of transport time (seconds)	Improved filling of small arteries	Increase in diameters main artery collaterals	
Thigh	4	1	++	8 52	1	2	++	10 60	
Calf	2	23	+(+1)	8 18					

Time between injection of contrast medium and appearance of early arterial filling phase

arteriography was repeated and in one patient was repeated again after another 17 minutes. In one patient (53 year old man) the effect of PGE_1 was compared with the effect of bradykinin. Ten $\mu\text{g}/\text{min}$ of bradykinin were injected during 10 minutes through the catheter and arteriography carried out. The patient then rested for about 15 to 20 minutes when he received a slow injection of PGE_1 followed by further arteriography. ECC was continuously monitored and from it the heart rate calculated. Arterial diameters were measured with a magnifying glass as described by ERIKSSON (1965).

Results

The diameters of the main arteries and of the collaterals always increased after the infusion of PGE_1 (Table) and an increased number of small peripheral branches of the arteries became evident (Figs 1-2). The transportation time for the contrast medium to the peripheral part of the leg always decreased (Table). The heart rate did not change and the electrocardiograms and blood pressure remained normal. Arteriography was again repeated 17 minutes after the end of injection of PGE_1 in a man aged 62 with arteriosclerosis. This revealed still an increased filling of the peripheral arteries.

A redness of the distal part of the leg was evident at the end of the injection of PGE_1 and persisted for nearly 30 minutes. No patients had side effects or complained of any discomfort.

The effect of bradykinin (Fig. 2) was the same as previously described (ERIKSSON 1965); the effects of PGE_1 and this compound were similar (Fig. 2, Table).

Discussion

Peripheral arteriography after PGE_1 resulted in increased contrast filling of the peripheral arteries. This effect was expected as it is known that PGE_1 increases the blood flow of the muscle and the skin. PGE_1 seems to have the same influence upon arteriography as bradykinin but is more persistent. PGE_1 caused no side effects in the concentrations used which agrees with previous results from infusions in man (CARLSON *et al.* 1968). The absence of side effects, the good vasodilatation and ease in use make PGE_1 a useful compound in peripheral arteriography. The results also justify consideration of the use of prostaglandins in other domains of arteriography. Previous investigation have indicated, however, that the vessels of the circle of Willis in man react little to the intra-carotid infusion of PGE_1 (STERNER *et al.* 1972).

Acknowledgements

The authors take this opportunity of thanking Prof S. Bergeron for his valued help. The bradykinin was kindly supplied by Sandoz AB.

SUMMARY

Prostaglandin E was infused intraarterially in a dose of 0.7 µg/min for 10 minutes before diagnostic peripheral arteriography. The result was an increase in the diameters of the main artery and collaterals. The demonstration of the small arteries was improved and no adverse effects were observed. PGE₁ may prove a useful compound in diagnostic peripheral arteriography.

ZUSAMMENFASSUNG

Prostaglandin E wurde intraarteriell in einer Dosis von 0.7 µg/min 10 Minuten lang vor einer diagnostischen peripheren Arteriographie infundiert. Das Ergebnis war ein Anstieg des Diameters der Hauptarterie und der Kollateralen. Die Darstellung der kleinen Arterien war verbessert und es wurden keine nachteiligen Effekte beobachtet. PGE₁ kann sich als nützliche Substanz bei der diagnostischen peripheren Arteriographie erweisen.

RÉSUMÉ

Les auteurs ont fait une perfusion intra-arterielle de prostaglandine E₁ à la dose de 0.7 µg/minute pendant 10 minutes avant une artériographie périphérique diagnostique. Le résultat a été une augmentation du diamètre de l'artère principale et de ses collatérales. La mise en évidence des petites artères a été améliorée et on n'observé d'effets nuisibles. La PGE₁ peut être un agent utile dans l'artériographie diagnostique.

REFERENCES

- BERGERON S, CARLSON L A and WILKES J R. The prostaglandins: A family of biologically active lipids. *Pharmacol Rev* 20 (1968) 1.
- BEVINGD S and ÖRS L. Effect of prostaglandin E₁ on forearm blood flow. *Scand J clin Lab Invest* 23 (1969) 347.
- CARLSON L A, EKLUND L C and ÖRS L. Clinical and metabolic effects of different doses of prostaglandin E₁ in man. Prostaglandins and related factors. *Acta med scand* 183 (1968) 423.
- — — Circulatory and respiratory effects of different doses of prostaglandin E₁ in man. *Acta physiol scand* 7 (1969) 161.
- ERIKSSON U. Circulation in traumatic amputation stumps. *Acta radiol* (1965) Suppl No 238.
- Effects of local intraarterial administration of bradykinin and hydralazine in obstructive arterial disease. *Acta radiol Diagnost* 10 (1970) 449.
- STRYER L, FORSTER D M C, BERGALL U and CARLSON L A. Effect of prostaglandin E₁ on cerebral circulatory disturbances. *Europ Neurol* 8 (1972) 23.
- WACKENHUT and BARTLEY O. Arterial spasm in peripheral arteriography using the catheter method. *Acta radiol* 47 (1957) 433.

MICRO GALLBLADDER AND BILIARY CALCULI IN MUCOVISCIDOSIS

H. ROSSIGNOL and A. SLOTH

Pathologic findings in the liver and biliary tract are well known in cystic fibrosis (mucoviscidosis, cystic fibrosis of the pancreas). Focal biliary fibrosis may be found in the liver at autopsy in nearly all children over one year of age (BODIAN 1952) and cirrhosis may sometimes be present (multilobular biliary cirrhosis with concretions) (DI SANT'AGNESE & BLANC 1956). The gallbladder may be hypoplastic and often have an obstructed cystic duct (BODIAN 1952). Histologically, numerous mucus-containing cysts appear in the submucosa whereas inflammatory changes are absent (ESTERLY & OPPEHEIMER 1962).

Only few reports on the radiologic examination of the biliary tract in cystic fibrosis are available: the most substantial work in this field was published by FRIJOLSON *et al.* (1970) and SAUVAGEOAIN & FENGELSON (1970). In 9 out of 30 cases, the gallbladder was smaller than normal, being 1 to 1.5 cm long and 0.5 cm wide for which these authors selected the term 'micro gallbladder'. The gallbladder was normal in 17 cases but failed to be demonstrated in the remaining 4 cases.

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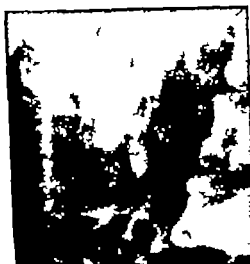


Fig. 1



Fig. 2

Fig. 1 Cholecystography. Micro-gallbladder in an 11 year old boy with cystic fibrosis

Fig. 2 Cholecystography. N demonstration of the gallbladder but filling of the biliary duct in 9 year old girl with cystic fibrosis

Material and Methods Radiologic examination of the biliary tract was performed in 45 patients suffering from cystic fibrosis. Four patients with no demonstration of the gallbladder by cholecystography were excluded as cholecystography had not been performed. The material thus consisted of 41 patients; the mean age was 10 years and 5 months with a range of 6 months to 23 years. Seventeen of the patients were girls. All patients were initially submitted to cholecystography with Panypaque, a sodium preparation of iopanoic acid in a dose of one tablet of 500 mg for children under 20 kg, two tablets up to 40 kg and three tablets for those up to 60 kg in weight. Children over 60 kg were given four tablets, the same dose as for adults. Cholecystography was performed in 19 patients in whom the gallbladder failed to fill with Biligradin 30 per cent, a methylglucamine preparation of adipodone in a dose of 1.5 ml/kg but never injected in doses over 20 ml. No side reactions were registered. Films were obtained every 20 minutes from 20 minutes after the injection until optimal demonstration of the gallbladder had been achieved; contraction of the bladder was then induced by a fatty meal. In the absence of filling the last film was obtained 3 hours after the injection (JONES et coll. 1958).

Results

The size of the gallbladder was regarded as normal when exceeding 1.5 cm to 2.0 cm in width and 3 to 4 cm in length (FRIEOLSON *et coll.*). The gallbladder was normal in size in 22 patients in 17 following cholecystography and in 5 only after cholegraphy. It was of definitely abnormal size in 6 patients in which it measured 0.5 cm to 1.5 cm in width and did not exceed 2 cm in length; the mean age of these patients was 13 years and 8 months (range 7 to 23 years). The term micro gallbladder proposed by SAUVEGRAN & FRIEOLSON has been used for this abnormality (Fig. 1). Exposures in different projections excluded a misinterpretation of a gallbladder of normal size in an axial projection. The outline was regular in all the gallbladders, including the micro-gallbladders and all contracted normally after a fatty meal.

No contrast filling of the gallbladder was obtained in 11 patients but in 3 of these the biliary ducts were normal in outline and size (Fig. 2). In 3 other patients the intravenously injected contrast medium appeared in the duodenum although no part of the biliary tract had been demonstrated in any of the films.

Two calculi were evident in a gallbladder of normal size in a 21-year-old girl; they had not caused symptoms. Stones were also likely in a male of 17 with symptoms and signs of cholecystitis, right abdominal pain radiating towards the right shoulder, choluria and abnormal liver function tests. Cholecystography suggested biliary stones but this could not be confirmed by cholegraphy.

Discussion

As most of the patients with cystic fibrosis have malabsorption of fat of a considerable degree it may not be entirely surprising to record an absence of filling at cholecystography in a large number of patients (19 out of 41). When the intravenous method was applied however pathologic conditions in the biliary tract usually appeared (14 out of 19 patients).

Micro-gallbladder in a considerable number of patients with cystic fibrosis (FRIEOLSON *et coll.*) has been confirmed in the present material. Cysts or other irregularities of gallbladder outline as demonstrated by the afore mentioned authors were not evident and the function of the bladders was normal. The patients with micro gallbladders were older than the remainder (mean age 13 years and 8 months and 9 years and 10 months, respectively). The small bladders were thus not a consequence of the relative size of the patients.

No filling or only partial demonstration of the biliary tract was obtained in 27 per cent of all the examinations. As the intravenous examination was generally performed several days after the administration of the oral contrast medium,

interaction between the media had presumably not been of importance in non filling of the gallbladder (CARTELL 1970)

The serum bilirubin was normal in all patients and occlusion of the main biliary tract was thus excluded. Furthermore the intravenously injected contrast medium was sometimes evident in the bowel but not in the biliary ducts. Whether the absence of contrast filling has any relation to the known liver lesion or to the biliary tract pathology in cystic fibrosis remains doubtful. Although elevated values of transaminases and alkaline phosphatases were often apparent, no significant correlation between these parameters and abnormal cholecystography or cholangiography could be demonstrated.

Three of the patients with cirrhosis of the liver had radiologic evidence of one micro-gallbladder, a gallbladder of normal size and one that failed to fill in spite of the outlining of apparently normal biliary ducts.

Gallstones with cystic fibrosis appear not to have been previously reported. Calculi that failed to produce symptoms occurred in a 21 year-old patient. Another patient with symptoms of cholecystitis may have had stones. Biliary calculi and cholecystitis may thus be one of the causes of abdominal pain in cystic fibrosis.

The clinical significance of a micro-gallbladder or nonfilling of the biliary ducts remains uncertain.

SUMMARY

Radiologic examination of the biliary tract in 41 patients with cystic fibrosis revealed changes in 19 consisting of micro-gallbladder in 6 and no filling or only partly filling of the biliary ducts in 11 patients. Gallstones were present in one and were probable in another patient. The clinical significance of micro gallbladders or the failure to demonstrate the biliary tract in these patients remains uncertain.

ZUSAMMENFASSUNG

Die roentgenologische Untersuchung des Galltraktes bei 41 Patienten mit zystischer Fibrose ergab in 19 Fällen Veränderungen bestehend aus einer Mikrogallenblase in 6 Fällen und fehlender oder teilweiser Füllung des Gallengangs in 11 Fällen. Gallensteine fanden sich bei einem Patienten und waren wahrscheinlich bei einem anderen vorhanden. Die klinische Bedeutung der Mikrogallenblase oder der Unmöglichkeit den Gallengang bei diesen Patienten darzustellen, erleidet Ungewissheit.

RÉSUMÉ

L'examen radiologique des voies biliaires chez 41 malades atteints de fibrose kystique montre des modifications chez 19 malades consistant en une microvésicule chez 6 malades et une absence d'opacification partielle des voies biliaires chez 11 malades. Il y avait des calculs biliaires chez un malade et il y en avait probablement chez un autre. L'importance clinique des microvésicules ou de l'absence d'opacification des voies biliaires chez ces malades reste incertaine.

REFERENCES

- ROSIAN M. I. *Brocyclic disease of the pancreas*. Heinemann, London, 1952.
- CATTILL W. R. Excretory pathways for contrast media. *Invest. Radiol.* (1960) 473.
- LEHRER J. R. and OLIPHANTER F. H. Observations in cystic fibrosis of the pancreas I. The gallbladder. *Bull. Johns Hopk. Hosp.* 110 (1962) 24.
- FERGUSON J. F. A. Y. and SALVESTRINI J. Liver function studies and biliary tract investigations in mucoviscidosis. *Acta paediat.* 59 (1970) 539.
- JOHN M. D., SAKAI H. and ROBERTSON A. C. Intravenous cholangiography in children with fibrocystic disease of the pancreas. *J. Pediatr.* 53 (1958) 172.
- DI SANTO AGOSTO L. A. and BLANC W. A. A distinctive type of biliary cirrhosis of the liver associated with cystic fibrosis of the pancreas. *Pædiatrica* 18 (1956) 317.
- SALVESTRINI J. et FERGUSON J. La cholangiographie dans la mucov. *Ann. Radiol.* 13 (1970) 311.

SIALOGRAPHIC APPEARANCES OF THE NORMAL PAROTID GLAND

SUNE ERICSON

The general paucity of information regarding the variation in the normal sialographic appearances of the salivary glands and the incidence of anomalies is mainly responsible for the difficulties in the differential diagnosis of congenital defects in these organs. One reason for this may be that sialography is seldom performed in patients free from salivary disease. Agenesis of one or more glands, ductal atresia, diverticula and congenital fistulas have however been reported (SCHREIBER 1927, STEGGERDA 1941, ANTHONY & FISHER 1948, LANTHROP 1956, SUNTHIEN 1960).

Among the conditions that both in the clinical and subclinical forms are generally regarded as abnormal and for which a roentgenographic examination may be of value are salivary calculi, atresia, segmented dilatation of the duct, duct diverticula, malactasia, fistulas, as well as deviations and destructions of the duct tree (PAYNE 1933, HETZAR 1947, ROSE 1954, OLLERENSHAW & ROSE 1957, GARINI 1964, PATEY 1965 and 1971, PREIFFER 1968, SCHULZ 1969, LAUDENBACH *et coll.* 1969). Other conditions that are manifested in hyperplasia or hypertrophy of the gland are more difficult to detect because of the wide

Table 1
Distribution of the series by age and sex

	Age group (years)				Total
	21-35	36-45	46-55	56-65	
Men	5	8	20	15	48
Women	8	21	33	30	92

normal variation in size. The work of ERICSON & HEDIN (1970) and ERICSON (1970, 1972, 1973) on the correlation between the size of the parotid gland *in situ* and the projected area of the gland in the sialogram has suggested a basis for such a diagnostic procedure.

Sialographic appearances are usually not characteristic. Especially in the initial stage or in subclinical variants as well as with widespread histologic changes in gland tissue it may be difficult to distinguish pathologic changes from anomalies or variants. A supplementary review of gland function may then be of help in clarifying the diagnosis. Tests of such function may be of value e.g. in various lipomatosis, sarcoidosis and atrophy, where the roentgenographic examination is usually negative (RUBIN & HOLT 1957; ENFORS 1962; SUNDVALL *et al.* 1966). A combination of sialography and a test of function would therefore presumably improve the possibilities of differentiating between normal and pathologic conditions. MAYNARD (1963) reported that the mean rate of salivary secretion was related to the sialographic appearances in chronic parotitis, and in the healthy subject ERICSON (1971) observed close correlation between the rate of secretion and the size of the parotid gland as represented in the sialogram.

The object of the present investigation was to examine sialograms of the parotid glands in a large number of clinically healthy subjects with no previous or existing signs or symptoms and, by correlating roentgenographic appearances with gland function, determine the frequency of anomalies.

Material and Methods

The investigation was performed in a group of patients attending for routine dental treatment. Apart from the exclusion of those with rheumatoid arthritis or diabetes or who were pregnant no selection was made. Of 150 requested to undergo the examination, 144 accepted. Each patient was interviewed and submitted to a clinical examination for diseases that might affect the salivary glands; the last 116 patients registered were also examined with respect to their



Fig 1 Parotid gland of moderate size with normal rate of secretion in proportion oblique lateral and a.p. projections. Contralateral gland similar in appearance.

general health and function of the parotid glands. With the exception of one patient, a chronic alcoholic who was excluded, none had any condition likely to produce changes in the glands.

There were no clinical signs of salivary gland disorders nor apart from subjective dryness of the mouth in some patients with normal parotid function were the histories indicative of changes. A detailed description of the clinical examinations have been given by ERICSON (1968) and ERICSON & JACOBSSON (1968).

Three patients in whom the sialographic examination was not completed were also excluded, giving a final material of 140 patients (Table 1). Right and left lateral sialograms were obtained in 135 patients and in the remaining 5 patients of one side only. 275 parotid glands in all were examined in this projection. Swelling and pain elicited by the initial lateral examination prevented it being followed by an a.p. view in 12 instances and in 8 it was employed only on one side. A total of 248 glands were thus examined in this projection.

Sialographic procedure. The examination of the parotid gland has been described elsewhere (ERICSON 1968, 1970). The central ray was directed at the middle of the gland — in the lateral projection at angles of 12° and 20° to the transverse plane of the head and in the a.p. projection perpendicular to the film plane and parallel to the ascending ramus of the mandible. A precision skull apparatus (Elema Schöer-Jer) at a FFD of 70 cm and about 3 cm be-

Table 2

Distribution of size of parotid glands in sialograms in lateral and p projections according to limits for normal variation \bar{x} = mean SD = standard deviation

	Lateral projection						A p projection							
	N of glands	Clands outside range						N of glands	Cland outside range					
$\bar{x} \pm 5D$			$\bar{x} \pm 2 \times 5D$			$\bar{x} \pm 5D$			$\bar{x} \pm 2 \times 5D$					
12.9-18.3			10.1-21.1			13.4-18.6			10.8-21.2					
		No		N				No		N				
Right side	137	40		6			123	41		3				
Left side	138	42		4			125	39		6				
Right + left sides	27	82	30	10	4		248	80	1	9	4			

tween the skin and the film in the lateral projection was employed. The contrast medium, Urografin 60 % was injected in a fractionated dose and sialograms obtained at three stages of filling. The injection was discontinued when the patient experienced moderate pain just in front of the ear. The amount of the agent injected varied with the size of the gland but never exceeded 12 ml.

The films were examined with special reference to the following points:

(1) The appearance and course of the ducts with the registration of deviations, destruction, concretions, sialectans, strictures and dilatation.

(2) The size of the glands and whether the area of projection in the lateral and a p views was within the adopted normal ranges, namely 10.1 to 21.1 cm and 10.8 to 21.2 cm for the respective projections (ERICSON 1970).

(3) The difference in size between the right and left glands: the maximum difference regarded as normal was 2.7 cm (ERICSON 1972).

(4) The maximum width of the parotid main duct, the ductus Stenon. It was decided whether the lumen in the lateral projection was within the normal range, namely 0.8 to 3.2 mm, with a largest individual left-right difference of 0.7 mm (ERICSON 1973).

(5) Retention of contrast medium in the ducts 5 minutes after the injection when according to RUSBY & HOLT (1957) and BLATT & MAXWELL (1957) it should have been evacuated.

The method of estimating the size of the parotid glands by sialographic and planimetric techniques was worked out by ERICSON (1968). ERICSON & HENRY (1970) in a methodologic investigation of autopsy specimens found that the



Fig 2a



Fig 2b



Fig 3

Fig 2 Two small glands in 2 subjects differing in appearance. The rate of secretion for the size was within normal limits. Opposite gland similar in appearance. a) Gland near the lower limit of the normal size range. Straight narrow main duct with few ramifications and greatest width centrally. b) Numerous ramifications of moderate calibre with greatest width centrally.

Fig 3 Parotid gland of slightly under average size with many ramifications and fine ductules. The main duct has maximum calibre of 0.8 mm. Opposite gland of similar appearance.

extent of the gland *in situ* may be represented in sialograms to an extremely high level of accuracy ($r=0.96$) and that practically linear relationship exists between the projected area of the gland in the lateral view and the total volume of the gland calculated after its removal ($r=0.95$). The lateral area of the gland may therefore be considered to represent its size. Close correlation ($r=0.80$ ERICSON, 1970) is evident between the projections of the parotid gland in the lateral and a.p. sialograms for a particular subject and likewise between the size of the right and left glands in these projections (ERICSON, 1972).

Test of gland function. The salivary secretion was measured after gustatory stimulation with 1, 6 and 10 per cent citric acid in the last 116 subjects examined by means of a method described by ERICSON (1968, 1971). The volume secreted was compared with the size of the area projected in the



Fig. 4. Two large glands in 2 patients with normal rate of secretion. a) The main duct with convoluted course and maximum width just less than the mean. The contralateral side is similar. b) Main duct with many ramifications and maximum width of lumen near the limit for the normal. Opposite gland similar.

lateral film with a ray direction of 12° and assessment made of gland function. The mean secretion and the normal limits for various sizes of healthy glands have already been defined graphically (ERICSON 1971).

Errors of the method. According to earlier analyses of methodologic sources of error the inter- and intrasubject differences in the interpretation of the sialograms were small. The precision and accuracy of the determination of size of the glands and the sialometric examination were high, especially compared with the intersubject variation (ERICSON 1968, 1970; ERICSON & HEDEN 1970).

Results

The sialograms of the parotid gland revealed a single main excretory duct issuing in the salivary papilla. The duct width varied within the gland, being greatest centrally and narrowing gradually in the proximal and distal directions. The lumen increased slightly at the points of ramification.

Large inter-subject differences existed in the pattern of the duct ramification: the number of branches and the length and width of the ducts. The branches were, however, narrower in the smaller glands. Primary, secondary and tertiary branches from the main duct were a normal feature. Quaternary branches were seen in a few glands with a wide main duct. Close right-left similarity in the glands of the individual subject was evident when the glands

Table 3

Distribution of comparisons between the left and right parotid glands in 135 subjects with respect to size of projected area in lateral sialograms. Standard deviation for the mean difference for the normal

	$< SD$ (1.8 cm ²)		$SD - 2 \times SD$ (1.8-2.7 cm ²)		$> 2 \times SD$ (2.7 cm ²)		Total
	No		No		No		
Right-left difference	114	83	15	11	6	4	135

Table 4

Maximum width of ductus Stenosi (mm) in lateral sialograms from 140 clinically healthy subjects distributed by normal ranges of variation. Mean \bar{x} and standard deviation SD

	Total	Gland outside the ranges	
		$\bar{x} \pm SD$ (1.4- 6)	$\bar{x} \pm 2 \times SD$ (0.6 3.2)
		No	No
Right gland	137	30	
Left gland	138	21	4
Right +left gland	27	51	9

Table 5

Maximum difference in width (mm) between right and left ductus Stenosi distributed with respect to ranges of variation. Mean difference (\bar{d}) and standard deviation of the mean difference SD

	Total	Gland outside the ranges			
		$\bar{d} \pm SD$ (> 0.4)		$\bar{d} + 2 \times SD$ (> 0.7)	
		No	No	No	No
Right-left differences	135	20	15	7	5

Table 6

Healthy subjects with clinically symptom free parotid glands but with sialograms differing from normal in respect of more than one factor

Case No. and sex	Age	I total projection						Spar- ran- tion from nor- mal	Reten- tion of contrast medium after 5 min	High or low — rat dis- cretion	Figure
		Deviation in size		Duct normality							
		Out- side normal range ($\bar{x} \pm 2$ SD)	R I diff out side normal range ($\bar{x} \pm 2$ SD)	Ma- jor duct width normal range ($\bar{x} \pm 2 < (\bar{d} \pm 1$ $> 5D)$	Sal- ivary duct ectasia ($\bar{x} \pm 1$ SD)	Stric- tures	regu- lar dia- meter				
1 M	58	R -						R	R	R -	11
		L						I	I	L	
2 M	60	L						I	I	not shown	9
3 F	59	L	x					L		L -	10
4 F	44				R	R			P	R -	8
										L -	
5 F	47				P				R	R -	-
6 F	61			I + x		I		L	L	L -	3
7 M	58	R -						R		R -	6
								L		L -	6
8 F	43							R	R	R -	7
								I	L	L	

were regarded as normal. Healthy glands of varying appearance and size are illustrated in figures 1 to 4, 8 d, 9 a, 10 a, 12 a and 13 a. The secretion of these glands was within normal limits.

Solitary or multiple constrictions with distal dilatations of the parotid main duct—segmentation—were evident in only 2 subjects (0.6 per cent) in both of them unilaterally. In one of these the gland had other duct anomalies and in the second patient the duct pattern displayed evidence of atrophy (Fig. 5 b). Retention of contrast medium was observed in both and the secretion was diminished (Table 6).

The terminal duct system differed distinctly from that in the rest of the material in 3 subjects (3 glands, 2 per cent): the duct ramifications on both sides



Fig 5



Fig 6

Fig 5 Gland with segmented main duct. Normal gland of opposite side

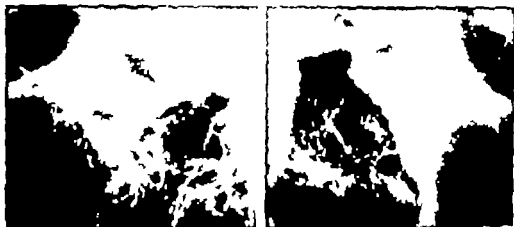
Fig 6 Small gland with irregularly disposed ducts. Contralateral gland of similar appearance. Low rate of secretion

forming an irregular pattern with short blunt terminal ducts (Figs 6 7 11 a). The gland function was again diminished in these patients with retention of contrast medium in the ducts 5 minutes after the injection was completed (Fig 7 c Table 6).

No deviations or destruction of the duct system were observed, nor were calculi nor zones free of contrast medium present in the parenchyma suggestive of infiltration, granuloma or other tumours or fat.

Punctiform accumulations of contrast medium adjacent to the ducts were observed unilaterally (0.6 per cent) in 2 subjects (1.4 per cent); in one they were numerous (Fig 8) with the main duct in this gland slightly dilated and segmented. The formations were apparent even before the duct was completely filled with contrast medium at low injection pressure. Pools of medium are consistent with the presence of sialectasis. Sialograms taken 5 minutes after the injection revealed pooling at the site of the previously registered formations (Fig 8 c). The rate of secretion was slow in relation to the gland size (Table 6).

The results of the examination of gland size are presented in Table 2. 96 per cent of the glands lay within what has been regarded as the normal range as measured in both lateral and a p projection. Figure 2 represents healthy glands with normal salivary secretion in size close to the lower limit of normality; figures 1 and 3 depict glands of medium size and figure 4 glands of large size also with the rate of secretion within normal limits. No significant difference between the sexes as regards the size of the parotid glands was evident.



b



Fig 7 a, b) Right and left gland in the same subject. The duct system is irregularly ramified and the terminal ducts are short and abrupt. The rate of secretion is low for this size of gland. c) Right gland 5 minutes after injection with retention of contrast medium in the ducts.

A right-left comparison of gland size in the individual subject is presented in Table 3. The area of 6 pairs of glands (4 per cent) in the lateral projection fell outside the normal limits: for 85 per cent of the pairs the difference was less than 1.8 cm²—that is, the mean difference plus the standard deviation. Three subjects (2 per cent) had a unilateral rudimentary gland: in 2 of them the other gland was within the normal range, while in the third it was below the lower limit (Figs 9, 10, 11). This gland also had an irregular duct pattern and a low rate of secretion. The rudimentary glands differed from the normal size by more than three times the standard deviation.

Table 4 demonstrates that in 97 per cent of the glands the width of the parotid main duct was within normal limits. The greatest width measured in the lateral

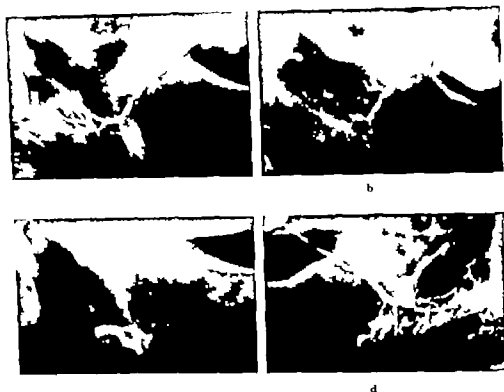


Fig. 8 Left parotid gland: low injection pressure. Small scattered punctate accumulations of contrast medium in contact with the ducts. b) Same gland: moderate injection pressure and complete filling. A few stiletatic formations are dispersed over the whole gland. The main duct is segmented. c) Same gland 5 minutes after injection. Punctiform accumulations of contrast medium similar in appearance and position to those in (b). d) Normal right gland. The maximum width of the main duct is at the upper limit of the normal range. Injection pressure the same as that in (b).

sialogram was 4.5 mm and the smallest 0.8 mm (Figs 3, 12). Nine (3 per cent) of the main excretory ducts exceeded 3.2 mm, the upper limit for normality according to the above definition. The deviation from the mean was more than three times the standard deviation in one instance (Fig. 12 b). Between men and women and between large and small glands a small but significant difference in the maximum width of the lumen existed. The excretory duct was on an average slightly larger in men than women (0.3 mm) and large glands had wider excretory ducts than small glands (0.4 mm). No correlation was observed between the variation in duct width and rate of secretion for glands of comparable size.



Fig. 9. Right and left gland in the same subject. a) Normal gland. b) Atrophied gland with low rate of secretion.



Fig. 10. Right and left glands in the same subject. a) Left gland normal. b) Right gland rudimentary with stage I development corresponding to that of 4 years of age.

Close agreement was evident between the duct lumina on the right and left sides (Table 5). The difference in 7 pairs of glands (5 per cent) lay outside the normal range, the greatest value being 1.1 mm, in which particular instance the main duct (Fig. 5) displayed other abnormalities.

Thirty-six glands (12 per cent) in 28 subjects (20 per cent) differed in at least one respect from what was defined as normal. Nine glands (3 per cent)



Fig. 11 Right and left glands in the same subject. a) Small gland with irregularly disposed ducts and low rate of secretion b) Rudimentary gland with main duct of ordinary caliber

deviated from the normal in at least two respects apart from gland function (Table 6)

Discussion

The roentgenographic appearances of the parotid gland vary with the extent to which it is filled with contrast medium. Opinions differ as to the optimal degree of filling. Several authorities consider the degree of filling aimed at in this investigation to be the optimal (RUBIN et coll 1955 GULLMO & BOOKE HYDERSTROM 1958 DIAMANT & FORSBERG 1959 BLATT 1964 ERICSON 1968) and that filling of the parenchyma is usually a diagnostic disadvantage (cf Fig 13) however this view is against that expressed by for instance OLLERENSHAW & ROSE (1957) and GARANI (1964) PFRIETER (1968) serial exposures in the dog as well as examinations in human subjects including biopsy and autopsy examinations have testified that filling of the duct system but not the parenchyma accurately reproduces size and subtle pathologic changes in the salivary glands (EINSTEIN 1966 ERICSON 1968 ERICSON & HEDIN 1970)

This investigation has produced no evidence of destruction or deviation of the duct system without contrast medium in a gland otherwise destroyed or calcified in the salivary ducts. This is consistent with the general view in textbooks and other publications (RAUCH 1959 GARANI 1964, 1965, 1968 SCHULZ 1969)

The size determinations disclosed large inter subject differences. All but 3 of the 10 glands outside the normal range of size, as judged from the area in the lateral projection had values near the limits ($< 2.5 \times SD$) and resembled in appearance the gland of the opposite side. Similar figures were obtained for the a.p. projection. These glands may be regarded as small or large, but healthy. In the 3 exceptional instances (Figs 9-10-11) the deviations in duct pattern size and secretion v. etc. so large as regards both the individual and the intra subject comparisons that the glands should be regarded as anomalous or pathologic. According to WIEDEMANN (1951) and PFEIFFER (1968) the development of the gland in figure 10 b corresponds to the normal at 4 years of age.

The absence of any age or sex differences in gland size and appearance is consistent with the findings reported by SURTHUIS (1960). The observations of HETZAR (1942), GAUWERAY & LINDEMANN (1948) and GARUSI (1964) that the duct system is finer and the glands are smaller in women than in men is thus not confirmed.

Large variations were present in the calibre of the parotid main duct both within the individual gland and between glands. The variation in the lumen of the excretory ducts might have been due in some measure to differences in injection pressure and possibly in the position of the glands in the beam. The standardized technique and the size of the series suggests however that any effect of these factors can hardly account for the large range of variation (0.8 to 4.5 mm). PFEIFFER (1968) and HETTWER & FOLSON (1968) in small series concluded that the duct lumen normally does not exceed 3 mm and 2.5 mm respectively and that the excretory duct widens towards its orifice while OLLENSHAW & ROSE (1951) stated that the normal calibre is some 3 mm. The present investigation indicates clearly that the duct lumen is largest centrally in the gland, and that 95 per cent of the duct lumina are between 0.8 and 3.2 mm in this region but that widths of up to 4.5 mm may occur in clinically healthy glands without other clinical or roentgenographic evidence of abnormality.

The conclusion reached by McCORMACK *et coll.* (1945) that 4 per cent of parotid glands have duplicate excretory ducts was not confirmed in the present investigation.

One gland had a segmented parotid main duct (Fig. 5) but unaccompanied by any anamnestic or clinical features. The unilateral location, retention of contrast medium in the duct and slow secretion rate in relation to the size of the gland pointed to an idiopathic or congenital change. Patients with idiopathic dilatation of the parotid main duct have previously been described by BARSON (1925), RICHARD (1937) and ROSE (1954).

The intraglandular ducts displayed polymorphism, with division into an increasing number of fine divergent branches which thinned out in a peripheral



Fig 12a



Fig 12b



Fig 13a



Fig 13b



Fig 13c

Fig 1. Two glands with maximum width of main duct. Opposite glands similar. Normal rate of secretion.

Fig 13. a) Large left gland with normal filling of ducts. Normal rate of secretion. b) Extravasation of contrast medium into parenchyma. c) Same gland 5 minutes after injection. Diffuse spread of contrast medium in the tissue. No similarity to sialectasis (cf Fig 8).

direction. The duct pattern evident in the sialograms presented large individual variations but, as with the parotid main duct, close similarity between the two sides was present. Obviously no consistent system of salivary ducts exists and a meaningful classification according to the pattern of ramification of the parotid tree as proposed by among others HETZAR (1942) AUBERT & GUZON (1949) and SUTHERIN (1960) would seem to be impractical.

While no obvious relationship was apparent between the sialographic appearance of the duct tree and the rate of secretion, the 5 glands with short abruptly ending and irregularly disposed ductules (Figs 6, 7, 11 a) displayed reduced function. MATZKER (1966) and SCHULZ (1969) have stated that cut off ending tuft shaped and slightly dilated end ductules as in these 5 glands are signs of age changes. GARUSI (1964) reported that the terminal ducts were irregular at advanced ages. SUTHERIN (1960) and PRIZFER (1968) on the other hand believed that the ramification and the width of the ducts do not serve as criteria of age changes, as the 5 glands from the 3 subjects in the present investigation confirm. The ages were around the mean for the group. The present results suggest that glands with the above appearance have a low rate of secretion irrespective of age. RAVON (1959) and SEIFERT (1966) found that age changes are manifested morphologically as acinar atrophy and lipomatosis. This means that sialography in practice affords little possibility of detecting age changes in the salivary glands.

Spherical pools of contrast medium adjacent to the duct system were observed in one gland of 2 patients (Table 6). When the formations appeared at a low injection pressure and with incomplete duct filling the pooling was probably indicative of true dilatation of the ducts. This was borne out by the retention of the water soluble contrast medium in the gland at the site of the pools 5 minutes after the injection was completed. These formations were similar in shape and size to those seen during the injection phase (Fig. 8). If they had been due to extraductal injection through a weakened epithelium as PATEY (1963) stated to be the cause of sialectasis the appearance of both the injection and retention phases (cf. Fig. 13) would have been different (the contrast medium was water soluble). The reduced secretion is another sign that the glands were defective.

The cause of sialectasis is a matter of opinion. It commonly occurs in various forms of parotitis as well as in a subclinical form in small children with manifest parotitis in the other gland (BAILEY 1945; CAMPBELL 1951; DECKER et coll. 1960; BLATT 1966; PATEY 1971). SMITH (1953) recorded radiologic evidence of duct dilatation in three generations of a family and PEARSON (1961) observed terminal duct dilatation with involvement of the main parotid duct in 2 pairs of siblings. Evidence of familial occurrence has also been reported in more recent literature (PATEY 1971). These observations indicated that sialectasis may be a

primary malformation analogous with cystic fibrosis or congenital bronchiectasis (ROSE 1954 RAUCH 1939 BECKER et coll 1960 GAROBI 1963 MATZKER 1966) KARLAY & SVIDER (1968) on the other hand held that parotitis in the newborn is a result of diarrhoea vomiting or other conditions leading to dehydration or cachexia PATEY (1971) recently stated that congenital sialiectasia is improbable No histologic or roentgenographic evidence that sialiectasia may be congenital has been presented Symptom free salivary glands with sialiectasia have, however been reported earlier in adults with rheumatoid arthritis (ERICSON 1968 WHALEY et coll 1968 CRUSHOLM et coll 1971) the cells displayed chronic inflammation with myoepithelial cell formations as in manifest Sjogren's syndrome

The sialiectasia in this series appeared in healthy individuals without clinical or serologic signs of either parotitis or collagenosis or of other diseases known to involve the salivary glands The glands were considered clinically healthy although the secretion rate was low for their size The formations in the 2 subjects were thus probably genuine and of congenital origin In the light of these observations and other evidence in the literature it would seem highly probable that sialiectasia may appear as a result of infectious autoimmune or congenital conditions

Congenital sialiectasia would thus appear to occur in a subclinical form in about 0.7 per cent of healthy adults the corresponding figure for subclinical sialiectasia in chronic rheumatoid arthritis has been previously calculated at 11 per cent (ERICSON 1968)

Twelve per cent of the whole series of glands displayed some deviation from the general sialographic image This high figure is due to the large number of factors registered simultaneously 4 of them based on statistical tests of probability As a confidence interval of 95 per cent was used and the deviations were largely solitary a single deviation should not necessarily be regarded as indicative of an abnormal gland If the limit for abnormality is taken as a deviation of the sialogram from the normal in at least two respects 8 abnormal glands in 7 subjects had a salivary secretion outside the normal range (Table 6) None of these or any other subjects presented anamnestic or clinical evidence of disease of the parotid glands

Whether the abnormalities in the sialograms should be interpreted as true anomalies changes due to aging pathologic states or the consequences of earlier disease could not be decided with certainty The negative morbid history together with negative clinical and serologic findings as well as the predominantly unilateral location indicate that 6 of the glands (2 per cent) may be regarded as true anomalies while the diagnosis in two instances (Cases 7 and 8 Table 6) is uncertain

SUMMARY

The sialographic appearances of the parotid gland have been examined in a large number of clinically healthy subjects without evidence of past or present salivary disease. The findings were compared with the results of an investigation of parotid gland function. The proportion of abnormal glands was found to be 2 per cent. The anomalies consisted in malformations of the main duct and terminal ducts and in the rudimentary development of the glands.

ZUSAMMENFASSUNG

Das sialographische Bild der Parotis wurde bei einer grossen Anzahl klinisch gesunder Personen ohne Zeichen einer vorangegangenen oder vorhandenen Erkrankung der Speicheldrüsen untersucht. Die Befunde wurden mit den Ergebnissen einer Funktionsuntersuchung verglichen. Der Anteil unnormaler Drüsen belief sich auf 2 Prozent. Die Anomalien bestanden in Missbildungen des Hauptganges und Endganges und einer rudimentären Entwicklung der Drüsen.

RÉSUMÉ

Les images sialographiques des glandes parotides ont été examinées chez un grand nombre de sujets cliniquement sains sans signe d'affection salivaire passée ou présente. Les signes ont été comparés avec les résultats d'une étude de la fonction parotidienne. La proportion de glandes anormales découvertes a été de 2 pour cent. Les anomalies consistaient en malformations du canal principal et des canaux terminaux et en développement rudimentaire des glandes.

REFERENCES

- ANTHONY D. H. and FISHER D. F. Diseases of the salivary glands and their ducts. *J. Tenn. med. Ass.* 41 (1948) 362.
- ALBERT J. A. et GLERU J. Diagnostic radiologique des affections des glandes salivaires. *Ref. Stomat.* 50 (1949) 255.
- BAILEY H. Congenital parotid sialiectasis. *J. int. Coll. Surg.* 8 (1943) 109.
- BÄCKMAYR T. Idiopathische Stenogangludilatation. *Klin. Wochschr.* 4 (1925) 2400.
- BACKER W., MATZEKE J. und RUCKEN J. Zur Morphologie der diffusen kugelförmigen Gangektasen in der Glandula Parotis. *Z. Laryng. Rhinol.* 39 (1960) 479.
- BLATT I. M. On sialiectasis and benign lymphonadenopathy. *Laryngoscope* 74 (1964) 1634.
- Chronic and recurrent inflammations about the salivary glands with special reference to children. *Laryngoscope* 76 (1966) 917.
- and MAXWELL J. H. Symposium. Disorders of the salivary glands. Secretory sialography. *Trans. Amer. Acad. Ophthalm. Otolaryng.* 61 (1957) 492.
- CAMPBELL V. A. B. Injunct parotitis in the newborn. Report of a case. *Lancet* 2 (1951) 366.
- CHENSOLOV D. M., BLAIR G. S., LOW I. S. and WATLEY K. Hydrostatic sialography as an index of salivary gland disease in Sjogren's syndrome. *Acta radiol. Diagnost.* 11 (1971) 577.

- DIAMANT H et FOSCHIERO A. La sialographie: méthode d'investigation de la glande parotéide. *Rev. Laryng* (Bordeaux) 80 (1959) 957
- ENSTED R. A. J. Sialography in the differential diagnosis of parotid masses. *Surg. Gynec. Obstet.* 122 (1966) 1079
- EWERUS B. The parotid and submandibular secretion in man. *Acta oto-laryng* (Stockh.) (1962) Suppl. No. 172
- EWERUS S. The parotid gland in subjects with and without rheumatoid arthritis. *Acta radiol.* (1968) Suppl. N. 273
- The normal variation of the parotid size. *Acta oto-laryng* (Stockh.) 70 (1970) 294
 - The importance of sialography for the determination of the parotid flow. *Acta oto-laryng* (Stockh.) 72 (1971) 437
 - Size of the normal parotid gland. *Acta radiol. Diagnosis* 12 (1972) 69
 - Width of the parotid main duct in healthy subjects. A sialographic investigation. *Acta radiol. Diagnosis* 14 (1973) 17
 - and HEDIN M. A clinical roentgenologic method of calculating the volume of the parotid gland. *Oral Surg.* 29 (1970) 536
 - and JACOBSSON E. A. A secretary and clinical investigation of the parotid glands in patients with rheumatoid arthritis. *Acta oto-laryng* (Stockh.) 63 (1968) 1
- GARBUS G. F. Swellings of the parotid region. Sialography as an aid in differential diagnosis. *Radiologie* 3 (1963) 364
- The salivary glands in radiological diagnosis. *Bibl. radiol. Fasc.* 4 (1964)
- GAUWERCK F. und LÖNNEMANN B. Erfahrungen mit der Sialographie bei Entzündungen und Tumoren der Parotis. *Röntgenpraxis* 17 (1948) 291
- GULLING A. and BOOR HEDERSTRÖM G. A method of sialography. *Acta radiol.* 49 (1958) 17
- HETTYER K. J. and FOLSON T. C. The normal sialogram. *Oral Surg.* 25 (1968) 790
- HETZER W. Die Sialographie. Georg Thieme Verlag, Leipzig 1942
- KARLAN M. S. and SYNDER W. H. Salivary gland tumors and sialadenitis in children. Experience at Children's Hospital of Los Angeles. *Calif. Med.* 108 (1968) 423
- LANTIERO E. D. Krankheiten der Speicheldrüse. *Laryngoscope* (St. Louis) 66 (1956) 251
- LA DEVRAGH P., BONCHAU M., MOREAU R. et BOURGEGRAVE C. Essai de séméiologie sialographique. *Rev. Stomat.* (Paris) 70 (1969) 19
- MCCORMACK L. J., CALLOWELL E. W. and ARMOR B. M. The surgical anatomy of the facial nerve, with special reference to the parotid gland. *Surg. Gynec. Obstet.* 80 (194) 620
- MATZKE J. Zur Parotis-Pathologie. Kugelförmige Gangektasien und Mischtumoren in der Ohrspeicheldrüse. *Z. Laryng. Rhinol.* 45 (1966) 450
- MAYNARD J. D. Recurrent parotid enlargement. *Brit. J. Surg.* 52 (1965) 784
- OLLERENSHAW R. G. W. and ROSE S. S. Radiological diagnosis of salivary gland disease. *Brit. J. Radiol.* 24 (1951) 532
- - Sialography—a valuable diagnostic method. *Mod. Radiogr. Photogr.* 33 (1957) 93
- PATRY D. H. Inflammation of the salivary glands with particular reference to chronic and recurrent parotitis. *Ann. roy. Coll. Surg. Engl.* 36 (1965) 26
- Recurrent swelling of the parotid gland (recurrent parotitis). *Mod. trends Surg.* 3 (1971) 261
- PAYNE R. T. Recurrent pyogenic parotitis. Its pathology, diagnosis and treatment. *Lancet* 1 (1933) 348
- PEARSON R. S. B. Recurrent swellings of the parotid gland. *Gut* 2 (1961) 210
- PREIFFER K. Handbuch der medizinischen Radiologie. Band VIII. Röntgendiagnostik der Weichteile. Springer Verlag, Berlin 1968

- RAUCH S Die Speicheldrüsen des Menschen Georg Thieme Verlag Stuttgart 1939
- RICHARD M Über Mukozelen der Parotis Helv med Acta 4 (1937) 679
- ROSE S S A clinical and radiological survey of 192 cases of recurrent swellings of the salivary glands Ann roy Coll Surg Engl 15 (1954) 374
- RUBIN P BLATT I M HOLT J F and MAXWELL J H Physiological or secretory sialography Ann Otol (St Louis) 64 (1955) 667
- and HOLT J F Secretory sialography in diseases of the major salivary glands Amer J Roentgenol 77 (1957) 575
- SCHÖLLNER H Rechtseitige Parotisaplasie bei linksseitiger Parotisdystopie Anat Anz 63 (1927) 842
- SCHULZ H G Das Röntgenbild der Kopfspeicheldrüsen Johann Ambrosius Barth, Leipzig 1969
- SENIERT G Mundhöhle Mundspeicheldrüsen, Tonsillen und Rachen Spezielle pathologische Anatomie J Springer Verlag, Berlin 1966
- SEWARD H P G HAMILTON D I and PATRY D H An investigation of the value in clinical practice of the curry test for parotid function Brit J Surg 53 (1965) 190
- SATTU M Familial incidence of sialactasia Brit med J 2 (1953) 1359
- STROGGERDA F R Observations on the water intake in an adult man with dysfunctioning salivary glands Amer J Physiol 132 (1941) 517
- SÜTTGEN G Ein Beitrag zur Auswertung von Sialogrammen der normalen Glandula parotis Medizinische Dissertation Leipzig 1960
- WHALEY A, CRIMMOLD D M, DOWNIE W W, DECK W C and WILLIAMS J Lymphocytic sialadenitis in the buccal mucosa in Sjogren's disease rheumatoid arthritis and other arthritides A clinical and laboratory study Acta rheum scand 14 (1968) 298
- WIEDENMANN H R Sialographie im Kindesalter Z Kinderheilk 69 (1951) 153

RENAL FUNCTION AT UROGRAPHY WITH COMPRESSION

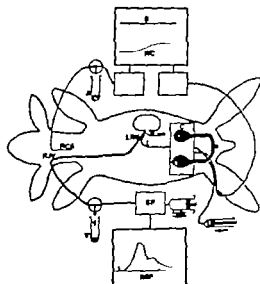
An experimental investigation in the rabbit

T B OLIN and D O REFS

Compression of the lower abdomen is widely employed as a means of producing stasis in the upper urinary tract at excretion urography with the purpose of accumulating the contrast medium in the pelvicalyceal systems. With no prior evidence of renal impairment the degree of pelvicalyceal filling is however sometimes poor despite compression sufficient to produce ureteric delay. The question then arises as to the extent to which the compression itself can produce changes in renal haemodynamics and function during the procedure. This was investigated in rabbits.

Materials and Methods Twenty seven Swedish land rabbits weighing between 1.5 and 2.8 kg were anaesthetised with intravenous pentobarbitone, all catheters being introduced under supplementary local anaesthesia to allow the level to be kept as superficial as possible. The left renal artery was catheterized from the femoral approach with a polythene catheter (OPP 60 Portex, England OD/ID 1.2/0.75 mm) with a thin tapered terminal curve (OD 0.35 mm). The tip was passed to a point just beyond the origin of the suprarenolumbar artery (ADAMS et al 1965). The left renal vein was catheterized from the right external jugular

Fig. 1. Experimental arrangement for determinations of renal blood flow and radiochemical extraction studies during compression. Key: I = spring driven injector pump; P = withdrawal pump; SP = spectrophotometer; RBF = indicator curve for renal blood flow recorded on the potentiometer writer; EM = electromanometer; BP and IVC = systemic arterial and inferior vena caval pressure tracings; RCA = right carotid artery; RJV = right jugular vein; LRA = left renal artery; LRV = left renal vein; C = compression device; A and V = sampling sites of renal arterial and venous blood.



vein with a soft polyvinyl chloride catheter (Ro 1 Portex OD/ID 1.6/0.83 mm) with two large side holes close to the tapered tip (EKELUND *et al.* 1972).

The systemic arterial pressure was continuously monitored electromanometrically (Mingograf 800 Siemens Elema Sweden) via a polythene catheter (PE 160 OD/ID 1.57/1.14 mm) in the right carotid artery and the venous pressure in the lower part of the inferior vena cava recorded through a narrow polythene catheter (PE 50 OD/ID 0.90/0.40 mm) (Fig. 1).

The renal blood flow was measured by an indicator dilution technique with indocyanine green (Cardio green). The renal artery catheter was primed to the tip with the indicator solution and 0.1 ml injected by a spring driven pump into the renal artery, the renal vein blood being withdrawn by a motor-driven pump at a rate of 0.11 ml/s and passed through the chamber of a spectrophotometer (Siemens-Elma). After analysis the blood was immediately reinfused by the pump to avoid disturbances due to blood loss; a small amount of heparin prevented clotting in the system. The concentration of the indicator in the venous blood withdrawn was recorded on a potentiometer writer (Servogor Goertz Austria) with a linear and a semilogarithmic channel to simplify extrapolation of the secondary slope of the indicator curve. The calculations of the renal flow, appearance times and mean transit times were made by the method of GOTTFRID & OLIN (1973). The apparatus was calibrated by adding measured amounts of the indicator to a sample of the venous blood and passing this through the spectrophotometer. In selected experiments determinations of the cardiac output

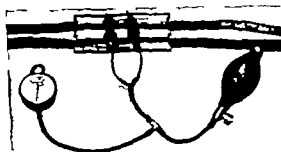


Fig. Compression device designed for rabbits

were also performed by injecting 1 ml indicator into one of the central veins and sampling from the aortic arch the speed of the withdrawal pump being increased to 0.25 ml/s

Two other parameters of renal function were evaluated with ^{51}Cr EDTA (ethylenediaminetetraacetic acid) and I hippuran. This combination of gamma radiation emitters allows simultaneous counting in a well scintillation detector (Selektromik Denmark). Tagged EDTA may be used in place of inulin as a measure of glomerular filtration and tagged hippuran with paraaminohippurate as a carrier to assess tubular secretion. The extraction ratios were determined from the radioactivity in samples of renal arterial (A) and venous (V) blood withdrawn simultaneously. Following counting the blood samples were reinfused into the animal. The clearance values (Cl) for ^{51}Cr EDTA were determined from the extraction ratio (E), renal blood flow (RBF) and haematocrit (H) according to the method of LINDAHL *et al.* (1970).

In the following formula b represents the background radiation at the gamma energy of the radionuclide

$$E = \frac{A - b}{A - b} \quad \text{and} \quad \text{Cl} = \text{RBF} \times E \times \left(1 - \frac{\text{Hct}}{100}\right)$$

Preliminary experiments in two animals determined the delay inherent in the catheter sampling recording systems. The catheters employed for the renal arterial injection and for the venous sampling were advanced from a femoral and a carotid artery respectively until they lay close to each other in the turbulent flow in the aortic arch. Indicator injections were made and the delays in the appearance times and mean transit times determined and allowed for in the subsequent calculations.

The recirculation component of the dye curve was then investigated after determinations of the left renal blood flow the arterial catheter was turned into the right renal artery and with sampling from the left renal vein alternating injections were made into the right and left renal artery.



Fig. 3 Urography with the compression device in position

Control animals were given 2 ml/kg Isopaque Cerebral intravenously (methyl glucamine metrizoate INN Nyegaard A/S Norway iodine content 280 mg/ml) and renal blood flow and extraction examinations made over a period of one hour. The effects of inferior vena cava and ureteric occlusion were then determined in the following manner.

A small balloon catheter (5 F Swan-Ganz flow directed catheter Edwards Laboratories U.S.A.) was introduced into the right superficial jugular vein and manoeuvred down into the inferior vena cava to a position below the termination of the left renal vein in 4 rabbits. The superficial jugular vein is formed in the neck of the rabbit by the union of two large tributaries, the anterior and posterior facial veins (MULLER 1922). This anatomic arrangement allowed both the balloon catheter and the renal vein catheter to be introduced down the same jugular vein. The balloon could be inflated to occlude the inferior vena cava and estimations of renal blood flow, cardiac output and renal function were made with and without occlusion. The left ureter was exposed in 4 animals by a retro-peritoneal approach and with a catheter connected to an electromanometer following occlusion the elevation in the intraureteric pressure was recorded.



Fig. 4. Obstruction of the superior renal calyx with collateral flow through the ureteral calyx.

Determinations of renal flow and function were made before and for 20 minutes during occlusion and also after release of the obstruction. An apparatus was designed for lower abdominal compression in the rabbit. A perspex plate (5 cm \times 14 cm \times 0.75 cm) was strapped to the anterior of the rabbit's abdomen so that two small balloons lying under the plate on either side of the midline could be inflated to compress the ureters; this is similar in principle to the Steinert compression device (STEINERT 1952) widely used in clinical urography in Scandinavia (Figs 2-3).

The renal blood flow and function were determined in 7 rabbits after an intravenous injection of contrast medium (2 ml/kg Iopaque cerebral). The positions of the two balloons were adjusted under fluoroscopy so that they lay just over the ureters. The balloons were then inflated to produce compression just sufficient to cause ureteric hold up, and further determinations made during

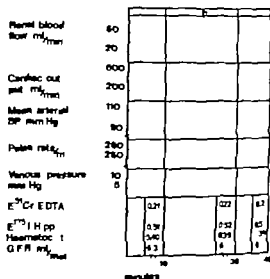


Fig. 5 Representative experiment with occlusion of the inferior vena cava.

a period of 20 minutes of compression and for 10 minutes following its release. Similarly blood samples were taken for the isotope determinations before compression, after 15 minutes compression and at 2 and 10 minutes after its release. The cardiac output in 3 of these animals was also measured and in a further 3 animals was determined without the renal function.

The effect of compression of the great vessels was investigated in 4 rabbits. Following inflation of the balloons at a pressure sufficient to produce ureteric hold up contrast medium was injected into the inferior vena cava via a femoral vein catheter and serial films exposed (Fig. 4). Similarly aortography was performed by retrograde catheterization of the femoral artery. Pressure recordings were also made at different levels in the abdominal aorta and on withdrawal of the catheter through the level of compression.

Finally in 4 animals pressure recordings were made through a catheter (PE 160 with multiple side holes) inserted in the peritoneal cavity of the upper abdomen: these were also obtained before and during the applications of compression.

Results

The indicator dilution curves obtained from injection into the left renal artery revealed a characteristic rapid initial deflection followed by a gradual return to the base line interrupted by a small secondary peak. When blood was again

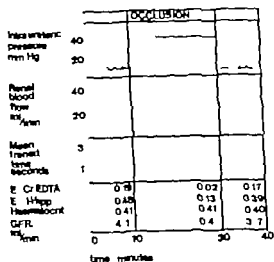


Fig 6 Representative experiment demonstrating the changes on ureteric occlusion

sampled from the left renal vein but with injections of the indicator into the right renal artery a small deflection was recorded and the timing and magnitude of this corresponded with the secondary peak of the renal concentration curve. This demonstrated that the phenomenon was produced by recirculation of the indocyanine green and that it did not represent a slow flow component. The method of excluding this recirculation deflection by extrapolation that has been devised by LINGARDH *et coll* (1969) for the calculation of the renal blood flow in dogs was thus also applicable in the rabbit.

The control experiments demonstrated that renal blood flow and the extraction parameters could be kept constant over a period of one hour providing that the superficial level of the anaesthesia was carefully controlled.

When the inferior vena cava was occluded by inflation of the balloon catheter no alteration in the renal blood flow (45 ± 12 ml/min) or the cardiac output (510 ± 80 ml/min) occurred apart from a small transitory fall in the pulse rate and systemic arterial pressure at the time of occlusion there was similarly no change in these parameters. The venous pressure was elevated from a value of 2 ± 0.5 mm to 7.5 ± 2 mm Hg and fell to the original level after deflation of the balloons (Fig 5). Occlusion of the left ureter produced an elevation of intra-ureteric pressure to a level of 42 ± 4 mm Hg. The renal blood flow presented only minor changes with a small increase from a value of 40 ± 6 to 47 ± 7 ml/min.

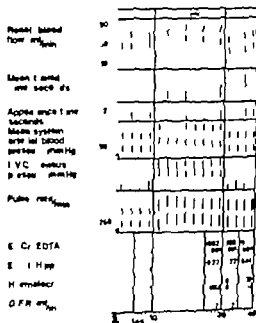


Fig. 7 The changes on abdominal compression with the mean values and the standard deviations.

No significant changes in the mean transit time (0.8 ± 0.2 s to 0.7 ± 0.1 s) were apparent. The extractions of ^{51}Cr EDTA and ^{125}I hippuric acid were depressed (21 ± 4 to 1 ± 1 per cent and 51 ± 5 to 12 ± 3 per cent respectively). Following release of the ureteric occlusion a marked fall in renal blood flow to 30 ± 5 ml/min and an elevation of the mean transit time to 3.1 ± 0.8 s occurred. Some recovery was evident with a flow value and transit time of 39 ± 6 ml/min and 1.5 ± 0.4 s at ten minutes. The extraction values for the radiochemicals had recovered although had not reached the preocclusion value (17 ± 2 and 40 ± 4 per cent) (Fig. 6).

The effect of the compression apparatus on the parameters of the renal function are displayed in figure 7. The compression produced an increase in the renal blood flow with an associated decrease in appearance and mean transit times. The extraction of ^{51}Cr EDTA was markedly impaired and there was also a fall in the extraction of ^{125}I hippuric acid. The mean arterial pressure and the pressure in the lower inferior vena cava were both slightly elevated. On release of the compression the renal flow fell below the original value with prolongation of the renal circulation times. Ten minutes after release the parameters of the renal function still presented some impairment in comparison with the original values.

The cardiac output fell slightly on compression to 91 ± 6 per cent of the original value with a recovery to 97 ± 3 per cent on release. Pressure recordings taken from the upper abdominal cavity demonstrated that the compression apparatus elevated the intraperitoneal pressure by only 2 ± 0.2 mm Hg.

Phlebography of the inferior vena cava established that compression sufficient to produce ureteric stasis occluded the former and would account for the elevation in venous pressure noted above. Aortography however revealed no evidence of narrowing of the aortic lumen and a withdrawal pressure tracing recorded no arterial pressure gradient at the level of the compression.

Discussion

General anaesthesia has been reported to decrease both the cardiac output and the renal blood flow in rabbits (NEUTZE *et coll* 1963). Intravenous pentobarbitone was however employed in the present material to produce only a superficial level of anaesthesia, and cutaneous pain sensation was abolished by supplementary local anaesthesia at the sites of approach. The flow values obtained compared favourably with those in unanaesthetized animals (KORNER 1963). The indicator dilution technique is an accurate method of obtaining repeated determinations of renal blood flow and provides additional information on renal circulation times (LINGGARDH *et coll* 1969). It does not involve the surgical dissection around the renal hilum required by the electromagnetic flow probe technique, and the catheters readily allow complementary chemical extraction examinations to be performed. STACY & THORNBURN (1966) and LINGGARDH *et coll* (1970) demonstrated that close correlation exists between the renal clearance of ^{51}Cr EDTA and a clearance of inulin. The ratio of the two clearances reported by LINGGARDH *et coll* was 1.041 when the plasma activity was calculated from the activity in whole blood corrected for the haematocrit value. This method of determining the glomerular filtration rate is of particular value in small mammals as the blood samples are not subjected to chemical analysis and can therefore be reinfused immediately after scintillation counting to avoid changes due to blood loss. The relation between the extraction of ^{125}I hippuran and PAH is less satisfactory with a ratio of 1.213. The extraction of the radiochemical is however employed as a parameter of tubular secretion: the difference is mainly due to the further fixation of the hippuran to the albumin fraction of the plasma.

External counter pressure over the abdomen has been reported to produce changes in renal function. BRADLEY & BRADLEY (1947) demonstrated a marked fall in effective renal plasma flow and glomerular filtration rate in man when the intraabdominal pressure was elevated by inflating a rubber bladder with air beneath a girdle applied to the anterior abdominal wall. SHENASKY & GILLEY

WATER (1972) have investigated the renal haemodynamic and functional effects of external counterpressure with a g suit in dogs. The experiments indicated that 80 per cent of an externally applied pressure of 30 mm Hg was transmitted to the retroperitoneal space and that this produced a marked fall in cardiac output, renal blood flow and the glomerular filtration rate. However, in both these previous investigations the counterpressure was spread over the entire abdomen and the situation differed markedly from the localized lower abdomen pressure applied during compression at urography. Many designs of compression apparatus are available to the diagnostic radiologist but the Steinert apparatus is the one most commonly used in Scandinavia. In this design a plexiglass plate is strapped to the lower abdomen and two pads lying under the plate on either side of the midline are inflated with air to produce localized pressure on the ureters and hold up the contrast medium. The miniaturized compression device employed in the present material is on a similar principle.

Abdominal compression in the present experiments produced a paradoxical increase in renal blood flow with shortening of the appearance and mean transit times. Glomerular filtration (the clearance of ^{51}Cr EDTA) had fallen markedly after 15 minutes compression and the extraction of ^{125}I hippuran was also impaired. These responses suggest that the major factor is the occlusion of the ureters. It should be noted that the intraperitoneal pressure in the upper abdomen was only slightly raised (2 ± 0.2 mm Hg) by the compression device in marked contrast to the elevation produced in the counterpressure investigations of BRADLEY & BRADLEY and SHENABAY & GILLENWATER and provides an explanation for the differences in the renal haemodynamic responses.

YOSHITOW SHI *et coll.* (1967) demonstrated a small increase in the renal blood flow on occlusion of the ureters in rabbits although the basal flow rates were low in relation to the weights of the animals, possibly related to the manipulations involved in the technique. This haemodynamic response to an elevation in intra-ureteric pressure of short duration has been previously recorded in dogs (NASH & SELAURT 1963). The present work with the indicator dilution technique established the same response to ureteric occlusion.

The compression device also produced a small fall in cardiac output which was not noted on balloon occlusion of the inferior vena cava. The possible explanation is that the compression caused not only an obstruction to flow in the vena cava but also a pressure gradient in the collateral paravertebral veins resulting in a diminished venous return to the heart. This diminished cardiac output however emphasizes the local renal haemodynamic response. Further it should be noted that both following release of abdominal compression and ureteric occlusion a transient fall in renal blood flow occurs with gradual recovery to the original values.

The circulatory complications of bradycardia and hypotension that have been recorded during compression urography in man and recently discussed by SVENDSEN & WILSON (1971) were not encountered in the present research.

These animal experiments have indicated that the application of lower abdominal pressure at urography produced changes in renal haemodynamics and function. In particular the roentgenologic value of this method of accumulating medium in the pelvicalyceal systems must be qualified by the knowledge that the glomerular filtration rate falls during compression, this being the sole pathway by which modern urographic contrast media are excreted by the kidney. A common practice is to apply compression five minutes after the injection in urography to allow some of the urine unmixed with medium to be cleared from the pelvicalyceal systems. However the fall in the glomerular filtration rate that occurs during the compression provides a further rationale for this delay. Further medium is sometimes injected if the filling of the collecting systems of the kidney is poor. The authors would suggest that if compression has been applied this should be released and that the further administration of contrast medium should be delayed for at least 15 minutes so that time will be allowed for recovery of glomerular filtration.

Acknowledgements

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SUMMARY

The effect of lower abdominal compression at urography on renal haemodynamics and function has been investigated in experimental animals. The relevance of the findings to clinical urography is briefly discussed.

ZUSAMMENFASSUNG

An Versuchstieren wurde der Effekt der Kompression des unteren Abdomens auf die Hamodynamik und Funktion der Niere während der Urographie untersucht. Die Anwendbarkeit der Resultate auf die klinische Urographie wird kurz besprochen.

RÉSUMÉ

Les auteurs ont étudié sur des animaux d'expérience l'effet de la compression de la partie inférieure de l'abdomen sur l'hémodynamique et sur la fonction rénale au cours de l'urographie. Ils examinent brièvement la possibilité d'appliquer les résultats de cette recherche à l'urographie clinique.

REFERENCES

- ADAMS D. I., OLIN T. and REFFMAN H. C. Catheterization of arteries in the rabbit. *Radiology* 81 (1965) 531.
- BRADLEY S. I. and BRADLEY C. I. The effects of increased intraperitoneal pressure on renal function in man. *J. Clin. Invest.* 26 (1947) 1010.
- FRISVOLD I., CÖSTEN J. and OLIN T. Arteriovenous fistulae in rabbit kidneys studied by a dye dilution technique and by angiography. *Scand. J. Urol. Nephrol.* 6 (1972) 81.
- CÖSTEN J. and OLIN T. Dye dilution technique with neptirion葡葡糖, especially for the determination of renal blood flow and related parameters. *Acta radiol. Diagnostica* 14 (1973) 113.
- KORNER I. J. Renal blood flow, glomerular filtration rate, renal PAH extraction ratio and the role of the renal vasomotor nerves in the unanesthetized rabbit. *Circulat. Res.* 12 (1963) 355.
- IMOLAARU C., MULLER T. and OLIN T. Renal blood flow in dogs studied by means of a dye dilution technique. *Scand. J. Urol. Nephrol.* 3 (1969) 281.
- — — 5 multineous determinations of renal blood flow and glomerular filtration rate without ureteric catheterization. *Scand. J. Urol. Nephrol.* 4 (1970) 232.
- MÖLLER F. *En Färdok i sjukvårdshjstens jämsförändringar* (In Swedish) 2nd edition, p. 265. Albert Bonniers Förlag, Stockholm 1972.
- NAVI J. D. and SIEKURT I. E. Renal haemodynamics during ureteral occlusion: the intact dog kidney. *Physiology* 6 (1963) 214.
- NEUFUR J. M., WYLLIE I. and RUDOLPH A. M. Use of radioactive microspheres to assess distribution of the cardiac output. *radius Amer. J. Physiol.* 21 (1965) 486.
- SHIMAZU J. H. and CHANOWAT R. Y. The renal haemodynamics and functional effects of external counterpressure. *Surg. Gynec. Obstet.* 131 (1972) 255.
- SRAOY B. D. and LINDBERG C. D. Chromium 51 ethylenediaminetetraacetic acid for estimation of glomerular filtration rate. *Science* 152 (1966) 1076.
- STENHART R. A compression apparatus for urography. *Acta radiol.* 58 (1967) 212.
- SUNDHOLM I. and WILSON J. Adverse reaction during urography and modification by atropine. *Acta radiol. Diagnostica* 11 (1971) 427.
- YOSHITOMI Y., HONDA N., MORIKAWA A., AIZAWA C. and SAKI Y. Alterations in intrarenal hemodynamics following changes in the ureteral pressure. *J. p. Heart* 18 (1967) 39.

CONTRAST FORMATION IN FLUOROSCOPIC VIDEODENSITOMETRY

II A comparison between theoretically computed and experimentally measured contrast

B. LANTZ and K. G. STRÖM

Videodensitometry is an accurate and fast method for determining the lumiance in a selected area of a roentgen television image in fluoroscopy (Wood et coll 1964 OSTERAA & HEINTZEN 1967). The method has been employed for determination of blood flow in central and peripheral circulation in connection with angiography (RUTISHAUSER et coll 1967 RUTISHAUSER 1969 SILVERMAN 1970 WOOD & STURM 1970 HEINTZEN 1971 LANTZ 1973). Extinction variations caused by an iodine contrast medium passing through a selected region of the object are measured. The measurement is performed in a small area of a television image recorded on magnetic tape in television fluoroscopy with fixed roentgentube voltage and current. Provided the exposure rate is kept constant throughout the investigation variations in the lumiance of the image provide a measure of the variations in the radiation extinction (i.e. absorption and scattering) by the object.

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According to the literature various tube voltage values and kinds of filtering have been used in videodensitometric blood flow measurements in order to obtain high contrast from the passing iodine contrast medium. If quantitative densitometric examination are to be based on extinction of the rays by a contrast medium three factors have to be taken into consideration viz the radiation source, the extinction process, and the detector system.

In Part I (STRID & LANTZ 1973) a mathematical model of contrast formation was given including the emission from the tube target, the extinction process and the conversion of the invisible roentgen relief into an image. In the present paper experimentally measured values will be compared with the computed contrast data.

The measuring system

A block diagram of the videodensitometric system used for blood flow examinations is shown in Part I (Fig. 1 p. 396). It consists of the roentgenologic basic equipment (including a television chain), the videodensitometer and a chart recorder.

The investigation was carried out with standard roentgenologic equipment (roentgen apparatus Triplex Angiomatix 1023/2 CE, Elema Schonander table Koordinat Kombi, Elema Schonander roentgen tube Rr 150/30/30 R, Siemens image intensifier Surecon 25/15, Siemens vidicon television chain Videomed I, Siemens). The videodensitometer used was constructed by T. Strand, Elema Schonander and B. Lantz. A multi channel strip chart recorder (Mingograf 800, Elema Schonander) served the purpose of recording the densitometer output.

Transmission of information from the object to the detector

The radiation emitted by the roentgen tube is attenuated by extinction (absorption and scattering) on passing the object, giving rise to the so called invisible roentgen relief. This relief is converted into a visible image on the entrance of the image intensifier. By electron optical means, the image is transmitted to the exit screen of the intensifier where it is reproduced diminished although with considerably increased brightness. The exit image is projected through an optical system on to the photocathode of the television camera, where the illumination density is determined at a large number of points along horizontal lines. The image information is contained in the video signal, which is transmitted to the television monitor where a similar image is formed.

Three links in this transmission chain are of interest when density variations in the object are to be measured (1) the extinction of the radiation by the object, (2) the transmission of the visible image through the image intensifier and (3) the transmission of image information through the television chain from the camera to the monitor

The extinction of radiation by the object For monochromatic radiation of wavelength λ passing perpendicularly through a layer of a substance of thickness t , the intensity of radiation transmitted through the exit surface of the layer is

$$I = I_0 \exp [-\mu(\lambda)t]$$

I_0 being the intensity of the incident radiation and $\mu(\lambda)$ (unit m^{-1}) being the linear extinction coefficient of the substance for radiation of wavelength λ . The quantity

$$E = -\ln(I/I_0) = \mu(\lambda)t$$

is the extinction by the layer for radiation of that wavelength. The linear extinction coefficient can be expressed in the mass extinction coefficient, $s(\lambda)$ (unit $\text{m}^2 \text{kg}^{-1}$) and the mass density ρ (unit kg m^{-3}) of the substance

$$\mu(\lambda) = s(\lambda)\rho$$

Thus,

$$I = I_0 \exp [-s(\lambda)\rho t] \quad (1)$$

which is known from optics as the Lambert Beer law. The extinction by a layer of substance is proportional to the density of the substance and to the layer thickness.

Alternatively, s may be the molar extinction (unit $\text{m}^2 \text{kmol}^{-1}$) and ρ the concentration of substance in chemical measure (unit kmol m^{-3}).

Linear density variations in an object inserted into a bundle of monochromatic roentgen radiation are thus reproduced as exponential intensity variations in the roentgen relief which appears as a visible image on the entrance screen of the image intensifier.

The image transmission through the image intensifier The luminance L (unit cd m^{-2}) of the image intensifier exit screen is a linear function of the exposure rate I (unit R s^{-1}) of radiation incident on to the entrance screen

$$L = G I \quad (2)$$

G being the conversion factor of the intensifier. Thus the information in any point of the roentgen relief is transmitted linearly through the image intensifier.

As pointed out by HOLM & MOURRY (1964) the sensitivity of an image intensifier tube varies over the spectral range the individual tube having its own spectral sensitivity maximum. This implies that the luminance of the exit screen at constant exposure rate, depends on the roentgen tube voltage and the filtering of the radiation. It appears that the conversion factor of a modern image intensifier tube reaches its maximum between 70 kV and 100 kV roentgen tube voltage with the total filtering of 22 mm aluminium.

The transmission of image information through the television chain. The electron beam of the television camera scans the image of the intensifier exit screen, directing it into 625 horizontal lines at the rate of 25 times per second. Each full picture scan (video frame) is composed of two alternately interlaced half picture scans (fields). The scanning electron beam gives rise to a video signal voltage S which is directly proportional to the luminance of the intensifier exit screen along the scan path. The signal is transmitted to the television monitor where the image is reproduced on the face of the display tube.

The video voltage varies linearly with the luminance of the intensifier output image

$$S = AI \quad (3)$$

A being the transfer function of the television camera.

Combination of equations (1), (2) and (3) yields

$$S \approx AG \cdot I \exp \{-\epsilon(\lambda) \rho t\} \quad (4)$$

Linear density variations in an object imaged in the radiation bundle are thus reproduced by exponential variations in the video voltage.

Image formation with polychromatic radiation. So far the roentgen radiation has been assumed to be monochromatic. Strictly speaking the radiation emitted by the anticathode contains photons of wavelengths from a cut off value λ_0 to infinity (cf. Part I). When the variation of the extinction and of the image intensifier spectral sensitivity with wavelength is taken into consideration (4) should be replaced by

$$S = A \int_{\lambda_0}^{\infty} s(\lambda) I_A(\lambda) \exp \{-\epsilon(\lambda) \rho t\} d\lambda \quad (5)$$

where I_A is the spectral intensity distribution with respect to wavelength and $s(\lambda)$ is the spectral sensitivity of the intensifier entrance screen.

The extinction coefficient varying with wavelength, the Lambert Beer law (eq. 1) is not applicable in the case of polychromatic radiation. Equation (5) shows that linear density variations in the object are generally not reproduced by exponential video signal variations. However it is often possible



Fig. 1. External view of the videodensitometers. The left instrument integrates the video signal directly, whereas the right one logarithmizes the signal before integrating.

to introduce an effective mass extinction coefficient $\bar{\kappa}$ for which the relation

$$S \approx \frac{AGI}{x} \exp[-x\bar{\kappa}]$$

holds. Especially the effective extinction coefficient of the contrast medium is related to the contrast function \bar{A} (cf. Part I)

$$\bar{\kappa} = \bar{A}t$$

The videodensitometer

The principles underlying the videodensitometer (Fig. 1) will be briefly presented here. A more detailed description will be given elsewhere (LAVTZ to be published).

In any particular area of the television image a rectangular sampling 'window' of optional size can be introduced by the operator. The densitometer output signal consists of the video voltage integrated along the scanning lines inside the window, thus being a measure of the integrated luminance in the sampling area. The video voltage is logarithmized before integrating, so that the densitometer output voltage V responds linearly to a linear change in the density of the object

$$V = k \int_{\text{area}}^{\text{sampling}} \ln S \, da \quad (6)$$

k being a constant pertaining to the logarithmator integrator and da denoting a surface element. From (4) and (6)



Fig. 2. The linear step wedge made from iodinated poly styrene.

$$I = k \int_{\text{area}}^{\text{sampling}} \ln AG_x I \, d\sigma = k \int_{\text{area}}^{\text{sampling}} e(\lambda) \rho t \, d\sigma$$

But $\int \rho t \, d\sigma = m$ is the total mass of substance in the object volume projected on to the sampling area and thus

$$I = I_0 - k e(\lambda) m$$

where I_0 summarises the dependence on $\ln AG_x$ and I_0 i.e. the densitometer signal varies linearly with the total mass of substance within the sample volume.

The measurements

The measurements were carried out with fine focus tube with a rhodium anticathode and an image intensifier with 12.7 cm entrance window diameter. The extinction of the radiation by an iodine step wedge was measured in a 5 cm \times 5 cm field well limited by diaphragms. The step wedge (Fig. 2) consisted of separate square plates of iodinated polystyrene which is resistant to roentgen radiation and heat (LANTZ & SÖRVIK 1973). The plates were plane parallel with an entrance surface of 12 mm \times 12 mm and 2, 4, 6, 8, and 10 mm thick ones. They were placed on the coordinate table so that they could be introduced one at a time into the roentgen ray field.

The sampling window of the videodensitometer was placed centrally in the field forming a square of 15 mm \times 15 mm. Great care was taken to ensure that the plate under examination was completely inside the window (Fig. 3). The position and size of the window remained the same throughout the measurements, nor was the gain of the strip chart record varied.

The luminance in the field outside the wedge was kept constant on changing tube voltage and filtering by setting the tube current so as to yield constant video white level which was determined from the strip chart record. The luminance was adjusted before the measurements by means of a cathode ray oscilloscope to yield optimal black and white levels in the video signal.

The extinction by iodine was measured roentgen tube voltage ranging from

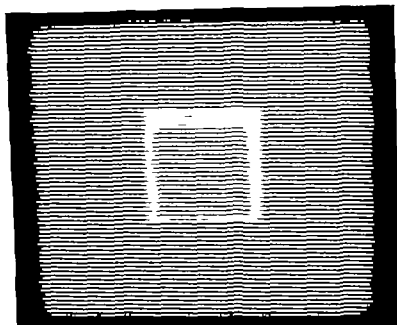


Fig. 3 The mon for image. The large bright area indicates the radiation field, the central bright area is the sampling window, and the darker area inside the window is the plate of iodinated polystyrene.

40 kV to 110 kV at 10 kV intervals. The radiation was filtered through water (0.5 or 10 cm) and copper (0.02, 0.4, 0.6, 0.8 or 1.0 mm) whereas the intrinsic filtration of the roentgen tube was equivalent to that of 2 mm aluminium. For each of the 92 measurements, the roentgen tube current was adjusted to give the same background luminance in the window area. The roentgen equipment used permitted a maximum tube current value of 5 mA, which precluded measurements to be carried out with low tube voltage and heavy filtering, since the required luminance value could not be achieved.

Results

The results are presented in Fig. 4, where the left column shows the computed contrast function k (cf. Part I) due to extinction by iodine for various values of the tube voltage U , provided that the screen luminance varies linearly with the exposure rate, whereas the right column shows the experimentally determined quotient $\Delta E/\Delta t$ between a step ΔE in the extinction and the causing step Δt in the thickness of the step wedge. The quantities k and $\Delta E/\Delta t$ are

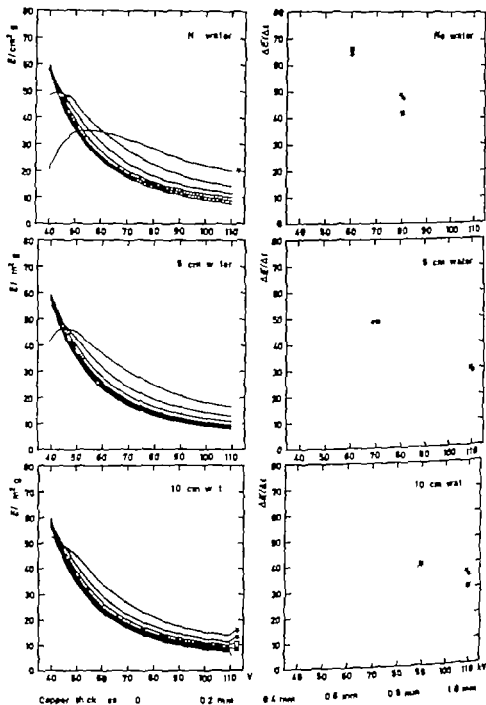


Fig. 4. Computed (left) and experimentally determined (right) effect of extraction coefficient of sodium for anode radiation filtering.

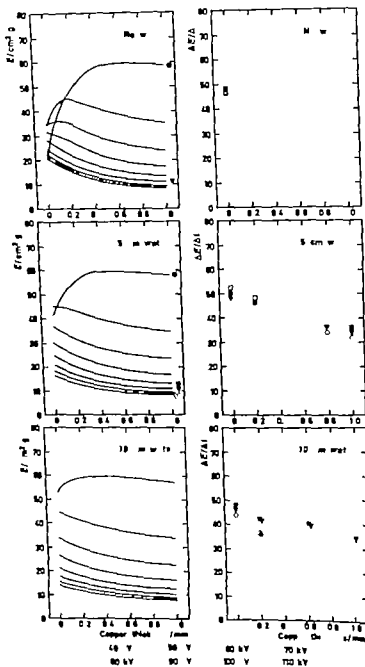


Fig. 5 The dependence of the computed (left) and measured (right) effects on the thickness of the copper filter for different iodine concentrations.

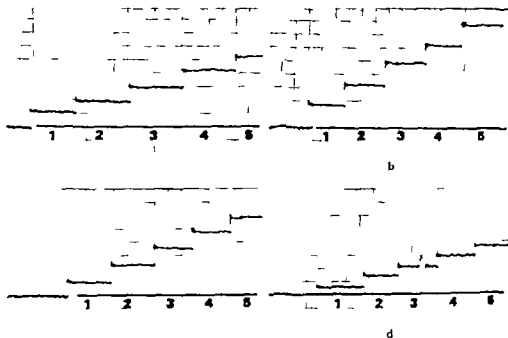


Fig. 6. Strip chart records of the x-ray densitometer output showing that the function of the amount of iodine in the step wedge of Fig. 2: a) 40 kV, 0.2 mm copper; b) 50 kV, 0.2 mm copper; c) 70 kV, 0.6 mm copper; d) 110 kV, 1.0 mm copper. The curves are linear.

proportional to each other but the factor of proportionality cannot be calculated since the iodine content of the step wedge was not known.

According to the mathematical model the contrast function reaches its maximum at 40 kV tube voltage. With water layers of 0.5 and 10 cm thickness maximum contrast occurs with 0.7, 0.5 and 0.4 mm copper filtering respectively (Fig. 4, left column). The tube current being insufficient to yield the required screen luminance at low tube voltage, no experimental data are available in the 40 kV region with copper filter (Fig. 4, right column).

The significance of filtering in the various series of computed and measured data is illustrated in Fig. 5. At 50 kV tube voltage and with no water layer contrast maximum according to calculations occurs with 0.2 mm copper filtering, well in agreement with experiment (Fig. 5, upper row). At 70 kV or higher contrast maximum always occurs with no copper filtering in model calculations as well as in experiments.

In all the 92 experiments the extinction was found to be a linear function of the amount of contrast substance in the step wedge (Fig. 6).

Discussion

On changing the tube voltage and the filtering between the experiments the image field background luminance was set to the same value by adjustment of the tube current. At constant tube voltage and filtering the luminance responds linearly to the exposure rate up to approx 160 mR s⁻¹ (HENN & BECKER 1961; BOSTROM 1969). The luminance also depends, however, on the quality of the roentgen radiation, i.e. on the tube voltage (HENN & BECKER 1961; HALZ *et al.* 1964; HOLM & MOSER 1964; GUYOT & DRIARD 1965). Each image intensifier has a sensitivity optimum which appears to occur for tube voltage in the range 70–110 kV. The λ absorption edge of iodine lies at 33.17 keV (BEARDEN 1967) and the contrast due to iodine is thus formed essentially by photons in the energy range 33–50 keV (cf. Fig. 3 in Part I). As regards the distribution of exposure rate in the invisible roentgen relief photons of energy above approx 50 keV contribute to the background without giving any significant contribution to contrast. However, introduction of iodine into the roentgen ray bundle shifts the photon energy distribution towards higher values, thus causing the conversion factor of the image converter G to increase. According to equation (2) a change in G and a simultaneous change in the exposure rate I give rise to a change in the luminance L of the entrance screen given by

$$\Delta \ln L \approx \Delta \ln G + \Delta \ln I$$

From the definition of the extinction one finds

$$\Delta E \approx -\Delta \ln I$$

Moreover from (3)

$$\Delta \ln L = \Delta \ln S$$

and from (6) assuming S to be constant over the sampling area

$$\Delta I = k \Delta \ln S$$

k being a constant. Thus the change in the videodensitometer output voltage due to the introduction of iodine is

$$\Delta I \approx k (\Delta \ln G - \Delta E)$$

Consequently, since $\Delta \ln G > 0$ in the case of interest here, the output voltage should be expected to fall more slowly with increasing tube voltage than is predicted by the simple model. The measurements show that this is the case.

The purpose of this investigation was to establish the correlation between extinction data as computed according to a mathematical model which does not

account for the spectral sensitivity of the individual detector and data measured experimentally by means of a specific detector system. The investigation has shown good agreement between the two sets of data. The variation in the experimental values can be explained by the inaccuracy of approx $\pm 2\%$ in the tube voltage setting.

In clinical measurements of blood flow in the extremities, a limited roentgen ray bundle is directed on to a region containing the examined vessel surrounded by soft tissue. The filtering due to soft tissue is comparable with that due to water layers of varying thickness up to 10 cm. The present investigation shows that copper filtering improves the contrast of iodine at low tube voltage (40–50 kV) but impairs it at higher tube voltage.

Conclusion

The experimental part of this work displays good agreement with the mathematical model. The latter can thus be used for optimizing the contrast in clinical work. In measurements with the tube voltage in the range 40–110 kV the extinction due to iodine as measured by means of the detector system specified varies linearly with the amount of iodine and the Lambert Beer law is thus applicable although the radiation is not monochromatic. When blood vessels in the extremities are examined by means of an iodine contrast medium, the best contrast is obtained at the lowest tube voltage value possible. In the voltage range 40–50 kV slight copper filtering improves the result. As far as optimal contrast is concerned it is recommended that angiographic examinations be performed at so low tube voltage as possible and with a 0.4 mm copper filter. A further investigation will show however whether this choice also minimizes the dose received by the patient.

SUMMARY

A mathematical model for the optimisation of roentgen contrast was presented in Part I (Strid & Lantz 1973). The extinction due to iodine was determined by a videodensitometric method for roentgen tube voltage values in the range 40–110 kV with copper filters and water layers of varying thickness. The agreement between the experimental data and the model is so good that the latter can be used for the optimisation of contrast in clinical diagnostic work.

ZUSAMMENFASSUNG

Ein mathematisches Modell für die Optimierung von Röntgenkontrast ist in I Teil (Strid & Lantz 1973) angegeben worden. Die Extinktion durch Jod wurde mit einer videodensitometrischen Methode für Röntgenrohren-Spannungswerte zwischen 40 und 110 kV mit Kupferfiltern und Wasserschichten verschiedener Dicke bestimmt. Die Übereinstimmung zwischen den experimentellen Daten und dem Modell ist so gut, dass letzteres für die Optimierung von Kontrast bei der klinischen diagnostischen Arbeit verwendet werden kann.

RÉSUMÉ

Les auteurs présentent dans la partie I (STRID & LANTZ 1973) un modèle mathématique pour l'optimisation du contraste radiologique. L'extinction due à l'iode a été déterminée par une méthode adéodensitométrique en fonction de la tension dans le tube roentgen entre 40 et 110 kV avec des filtres de cuivre et des couches d'eau d'épaisseur variable. La concordance entre les données expérimentales et ce modèle est si bonne qu'on peut utiliser ce modèle pour l'optimisation du contraste en radiographie clinique.

REFERENCES

- BRADEN J. A. X-ray wavelengths. *Rev. mod. Phys.* 39 (1967) 78.
- BOSTROM U. Investigation of x-ray image intensifier tubes. Research Laboratory of Medical Electronics, Chalmers University of Technology, Göteborg 1969.
- GUYOT L. F. et DELIAUD B. Développement récents dans le domaine des amplificateurs de luminescence radiologiques. *Rev. Techn. CITH* 42 (1965) 55.
- HALE J., EPPERSON R. D., GEORGE D. L. and TRIST A. Physical factors in cinefluorography. *Amer. J. Roentgenol.* 92 (1964) 1192.
- HELVETZ P. H. Roentgen cine and adeodensitometry: fundamentals and applications for blood flow and heart volume determination. Georg Thieme Verlag, Stuttgart 1971.
- HENRY G. C. and BACKER J. A. Comparison of the light output of image intensifier tubes. *Radiology* 77 (1961) 472.
- HOLM T. and MORELL R. D. The conversion factor for image intensifiers. *Radiology* 82 (1964) 898.
- LANTZ B. A methodologic investigation of roentgen videodensitometric measurement of relative flow. To be published as 9 pp. to *Acta radiol.*
- and SÖDERIK I. Use of iodine containing polymers for calibration and absorption measurements in radiography. *Acta radiol. Diagnosis* 14 (1973) 729.
- ÖVERA P. and HELVETZ P. New applications of television techniques for quantitative measurements in radiology and cardiology. Digest 7th Internat. Conf. Med. Biol. Eng. Stockholm 1967.
- RUTTENHAUER W. Kreislaufanalyse mittels Röntgendensitometrie. Verlag Hans Huber, Bern 1969.
- , SIMON H., STUCKY J. P., SCHAN N., NORD G. and WELLAUER J. Evaluation of roentgen cine-densitometry for flow measurement in models and in the intact circulation. *Circulation* 36 (1967) 951.
- SILVERMAN N. R. Television fluorodensitometry: technical considerations and some clinical applications. *Invest. Radiol.* 5 (1970) 33.
- STRID K. G. and LANTZ B. Contrast formation in fluoroscopic videodensitometry. I. A mathematical model for optimizing contrast in radiography. *Acta radiol. Diagnosis* 14 (1973) 39.
- STURM R. E., SANDERS J. J. and WOOD E. H. A roentgen adeodensitometer for circulatory studies. *Fed. Proc.* 23 (1964) 303.
- WOOD E. H. and STURM R. E. Use of videometry and electronic data processing for hemodynamic investigations by angiographic techniques. In: *Pathophysiology of congenital heart disease*. Edited by P. H. Adams, H. J. C. Swan and V. E. Hall. Univ. of California Press, Los Angeles 1970.
- and SANDERS J. J. Data processing in cardiovascular physiology with particular reference to roentgen adeodensitometry. *Proc. Mayo Clin.* 39 (1964) 849.

CLINICAL EVALUATIONS OF A HISTOLOGIC EXAMINATION OF THE SIDE EFFECTS OF MYELOGRAPHIC CONTRAST MEDIA

J. H. JAKOBSEN

Side effects following myelography with positive contrast media have been reported with varying frequency and have usually been ascribed to meningeal reaction. An experimental histologic examination of the spinal and nerve roots and meninges after myelography with iodophendylate and methiodal was undertaken.

The results of this investigation will be briefly summarized with special reference to the roentgenologic findings. Comparison will be made to complications in myelography in human subjects and precautions necessary in this procedure will be suggested.

Results

Iodophendylate Thirty four rats weighing 250 ± 40 g were injected with 0.15 ml iodophendylate (Pantopaque) by suboccipital puncture. The amount was calculated to the proportional weight of the spinal cord in rats and men and

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related to the employment of 10 ml iodophendylate in human myelography. Three rats were injected with 0.015 ml iodophendylate—a dosage that accepts that a tenth of the contrast medium used for myelography in human subjects remains in the subarachnoid space. In a third group 0.075 ml blood was added to 0.075 ml iodophendylate in 19 rats. Histologic examination of the structures in the spinal canal was performed at 1, 4, 8, 16, 30, 60 and 120 days. bacteriologic controls were also included.

One hour after the injection the contrast medium was seen to lie in a unilateral column up to the level of the second lumbar vertebra while along the remaining part of the spinal cord unconnected thin lines were situated. In the posterior fossa droplets of contrast medium were evident. The column of contrast medium later broke and appeared as droplets opposite the intervertebral foraminae. After 16 to 30 days half the injected iodophendylate became apparent. No further reduction in the quantity of contrast medium was observed from the 30th to the 120th day but after 120 days droplets of iodophendylate were present opposite the intervertebral foraminae in the lumbosacral region and the posterior fossa. The rats were clinically inactive the first days after the injection of contrast medium but were without any signs of paralysis, and without any further signs during the rest of the experimental period.

In all animals the microscopic appearances of the leptomeninges presented a moderate unspecific inflammation which was most marked around vessels and nerve roots in the lumbosacral region. Infiltration with neutrophilic leucocytes first appeared to be followed at 120 days with eosinophilic leucocytes. Fibrosis predominated at 30 days. The injection of blood and iodophendylate caused meningeal reaction which was a little more marked and started earlier but after 120 days no quantitative differentiations from rats injected only with iodophendylate were apparent. Slight to advanced fibrosis of the endo- and perineurium in the nerve roots and from the 8th day a little to moderate degeneration of axons and myelin sheaths was evident. Moderate vacuolization and an increasing loss of neurons in the spinal cord were observed within the first month. By reducing the amount of iodophendylate to 0.015 ml the damaging effect on the grey matter was avoided. The decreased dosage of iodophendylate failed to change the meningeal reaction to any significant degree.

Methodal. Ninety rats were injected with methiodal (Conturex) and 55 died after a few minutes. 3 to 10 seconds after the injection of medium into all the animals anaesthetized with nembutal tonic spasms followed by clonic cramps developed. Methiodal was not sufficiently dense for demonstrating the spinal canal of the rats. At 6 hours, 1 day, 4, 8, 16, 30 and 90 days after the injection the surviving animals were killed.

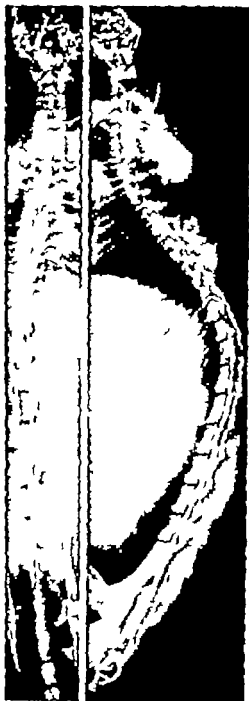


Fig. 1



Fig. 2

(For legends see opposite page.)



Fig 3 Fibrosis of the leptomeninges 120 days after the injection of only iodophendylate. The membranes round the nerve roots are thickened and fibrous scarring in the arachnoid is evident (top). Haematoxylin and eosin $\times 125$.

The microscopic appearances of the meninges disclosed signs of slight inflammation that did not differ from alterations observed in rats injected with physiologic saline. All structures of the spinal canal presented a slight but general perivascular extravasation of erythrocytes, and in several rats moderate degenerative alterations of the anterior spinal artery were noted. Acute swelling and an extreme vacuolization of the nerve cells with vacuoles measuring up to 100 microns were present in the grey matter of the spinal cord. The number of nerve cells had decreased at 8 days and any further alterations in the following groups failed to occur. Foci of moderate degeneration and disorganization in the white matter and a slight degeneration of the myelin sheaths of the nerve roots were recorded.

Five control rats injected with physiologic saline had slight changes in the white and the grey matter. Histologic alterations quantitatively not exceeding those not present in the control group have not been described.

Discussion

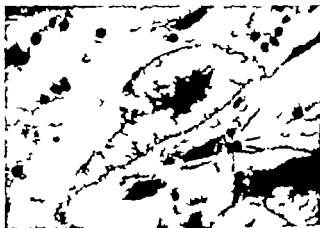
Iodophendylate. The irritative and aseptic arachnoiditis produced in experimental myelography with iodophendylate was in good agreement with that described by other authors (16, 17, 26). Fibrosis of endo- and perineurium of the nerve roots, however, has not been dealt with.

Meningeum. among the clinical descriptions of complications after iodophen-

Fig 1 Contrast medium in unilateral column up to L₄ and as droplets in the posterior fossa one hour after the injection of iodophendylate into the subarachnoid space.

Fig 2 The amount of contrast medium is reduced 140 days after the injection of iodophendylate into the spinal subarachnoid space. Droplets lie opposite the intervertebral foraminae and in the posterior fossa.

Fig. 4. Nerv. cells from the cervical part of the spinal cord 4 day after the injection of methiodal. A swollen nerve cell lies at the centre of the figure with a shrunken one beneath it. Toluidine blue $\times 500$.



dylate myelography in man, is frequently reported. A slight increase in the number of cells from the spinal fluid of all the patient examined has been reported (PEACHER & ROBERTSON 1945; BELANGER *et coll.* 1958) and arachnoiditis probably caused by iodophendylate has been confirmed in several cases after an operative or autopsic procedure (7, 13, 18, 21, 27).

Radicular and neuralgic pain and aching across the loins may arise after the myelography (2, 7, 27) and are said sometimes to increase and persist (2, 7, 13, 27). A relation between radicular pain and the cellular reaction in the spinal fluid was suggested by BELANGER *et coll.* (1958) and SEIGAL *et coll.* (1967). A possible confirmation for this was the endoneurial reaction and fibrosis of the nerve roots observed in this experimental investigation.

Little attention has been accorded to the state of the spinal cord after experimental myelography with iodophendylate. Several experimental investigations have been concerned with alterations in the grey matter in the period of lipiodol (1925 to 1945). Loss of nerve cells and shrunken nerve cells with vacuolization of the cytoplasm have been reported by PEIPER & KLOSE (1925), BRUSHY & PROPPER (1931), DAVIS *et coll.* (1930) and BOLDREY & AIRD (1944), and in the present series the decrease in the number of nerve cells was regarded as dependent on the amount of contrast medium (PEIPER & KLOSE 1925; OCHOA 1942). It should be observed that it was impossible for HEMPEL & ZETTLER (1965) to demonstrate any quantitative or qualitative differences between the meninges of animals injected with pantopaque or lipiodol.

To the knowledge of the author the only paper that deal with the histologic appearances of the spinal cord following myelography in human subjects is the one by MASON & RAAR (1962). Four ml of contrast medium remained in the subarachnoid space of a patient who died 7 months after a pantopaque myelo-

graphy. The post mortem examination disclosed complete obliteration of the subarachnoid space by a membrane 1 to 10 mm thick. extensive vacuolization throughout the outer two-thirds of the spinal cord and parts of the cerebral hemispheres was evident. Numerous fat laden phagocytes were present but no bacteria, abscesses or areas of necrosis were observed.

Paralysis and paresis are in human beings complications that have sometimes been reported as sequelae of pantopaque myelography (7 11 21 27 30). retention of urine has also been recorded (7 21 22 24). Cranial nerve palsies are by some authors ascribed to the meningeal reaction, but it is possible that these are caused by a toxic effect of the medium. This experimental investigation failed to establish whether the damage to the grey matter of the spinal cord was brought about by a toxic effect or was secondary to the inflammation of the meninges.

Methodol. Comparison of the few papers concerned with histologic alterations after experimental myelography with methiodal is difficult as the animals were reacting in a clinically differing manner and because some authors have added spinal anaesthesia to the medium.

A smaller amount of methiodal than used in the paper on the histology of the condition as yet unpublished produces a slight alteration only in the brain of rabbits (SCHONER 1964). Severe damage to the white matter of the spinal cord was observed by FURUKAWA & OUEL (1961) after injection of methiodal and spinal anaesthesia although the histologic appearances of the grey matter were not described.

Complications reported in relation to myelography with methiodal as well as with iodophendylate in man may sometimes be ascribed to the lumbar puncture itself, a wrong technique, the spinal anaesthesia or to an accidental aggravation of the disease. Headache and slight rise in temperature are frequently noted in relation to the employment of water soluble media, but meningism is seldom observed. Information concerning a chronic state of fibrous scarring to any significant degree has never been given.

A remarkable and frequently reported side effect is tonic and clonic spasms of the legs appearing 2 to 3 hours after the investigation. the condition may develop into epileptic seizures (3 10 19 20 23 31). A persistent decrease in sensitivity (3 15 19 25 28), paralysis of the legs or temporary loss of tendon reflexes (3 10 19 31), paresis of the bladder (3 19 23) and impotence (3 9 19) have been reported as side effects following the use of methiodal.

These clinical observations render probable a damaging effect of the medium on the spinal cord or the nerve roots. Electrophysiologic investigations in cats support such a supposition (HARVEY et coll 1961). Both the histologic results obtained in the investigation by FURUKAWA & OUEL (1961) and in the unpublished paper pointed out the alterations in the spinal cord as the most salient

feature, whereas the changes in the nerve roots were probably of minor histologic importance. This is in accordance with the clinical observation of AHLGREN & PRÆSTIÖLM (1969) who observed an increased frequency of muscle spasm when the level of contrast medium reached the spinal cord.

The nature of the damaging effect on the medullary parenchyma in this work is presumably of a vascular or a toxic origin, in good agreement with the results obtained by FUNAQUIST & OBEL. The acute swelling of the nerve cells observed is a characteristic feature of acute intoxication (SPIELMEYER 1922; GREENFIELD 1960) so that the toxic property of methiodal to the neurons is emphasized.

Conclusions

The performance of pantopaque myelography results in an inflammation of the leptomeninges even if the bulk of contrast medium be removed after the investigation and even if admixture of blood to the contrast medium be avoided. The possibility furthermore cannot be excluded that larger amounts of pantopaque have a damaging effect on the spinal cord. Clinical observations and experimental investigations render probable a toxic action of methiodal on the spinal cord. The amount of pantopaque used should be kept as small as possible. Care must be taken with methiodal to try to prevent it from reaching the level of the spinal cord.

SUMMARY

Histologic examination as yet unpublished of the spinal cord, nerve roots and meninges in rats after myelography with iodophendylate (Pantopaque) or methiodal (Conturex) is briefly summarized. Complications reported clinically are compared. Both media possibly exert a damaging effect upon the spinal cord.

ZUSAMMENFASSUNG

Es wird ein kurzer Überblick gegeben über bisher unveröffentlichte histologische Untersuchungen des Rückenmarkes, der Nervenwurzeln und der Meningen nach orthograde Myelographie mit Jodophendylat (Pantopaque) und Methiodal (Conturex). Die Resultate werden mit klinisch berichteten Komplikationen verglichen. Es ist möglich, dass beide Substanzen schädigend auf das Rückenmark einwirken.

RÉSUMÉ

L'auteur résume brièvement l'examen histologique jusqu'ici non publié de la moelle épinière, des racines nerveuses et des meninges au des rats après myélographie avec l'iodophendylate (Pantopaque) ou le méthiodal (Conturex). Il rapproche ces aspects histologiques des complications décrites cliniquement. Il est possible que ces deux moyens de contraste exercent un effet nocif sur la moelle épinière.

REFERENCES

1. ARTHURSEN I. og FRILSTEDT J. Komplikationer ved myelografi med methiodalum. Nord Med 82 (1969) 1600
2. BELANGER C. ROY C. DROLET M. et HÉON M. Le liquide céphalo-rachidien après injection sous arachnoïdienne de pantopaque. La al méd 26 (1958) 607
3. BÉTOULIERE P. TEMPLER J. P. et JAMNOT J. Y. La radiculographie lombo-sacrée u methiodal. J. radiol. Électrol 41 (1960) 447
4. BOLDREY E. and AIRD R. B. The effects of iodized poppyseed oil and sodiumchloride in peanut oil in the subarachnoid space of animals. J. nerv. ment. Dis 99 (1944) 521
5. BRUNET J. und PROBYER N. Experimentelle Myelo-encephalographie an Hunden und über den Einfluss von Jodipen und Lipoydol auf das Rückenmark. Gehirn und dessen Hülle. Z. ges. exp. Med 75 (1931) 54
6. CRAIG R. L. Effect of iodized poppyseed oil on the spinal cord and meninges. Arch. Neurol. Psychiat. 48 (1942) 799
7. DAVIES F. L. Effect of unabsorbed radiographic contrast media on the central nervous system. Lancet 1936 II 747
8. DAHL L. HAYDEN H. A. and STONE T. T. The effect of injections of iodized oil in the spinal subarachnoid space. J. Amer. med. Ass. 94 (1930) 772
9. DIETZ H. und ULBRUCHT W. Zur Frage der Potenziierungen nach lumbarer Myelographie mit positiven Kontrastmitteln. Acta neurochir. 19 (1968) 109
10. FERRAND J. D'ESMOLDES J. R. et BARSOTTI J. La radiculographie lombo sacrée par substance iodée hydrosoluble et résorbable. Exposition scientifique française. Paris 1961
11. FINCHAM R. W. JOYNT R. J. and SKILLITY F. M. Neurological deficits following myelography. Arch. Neurol. 16 (1967) 410
12. FURUKAWA B. and OMEL N. Effect on the spinal cord of subarachnoid injection of water soluble contrast media. Acta radiol. 56 (1961) 449
13. GAUTRIER G. Les accidents de la myélographie avec produits de contraste non résorbables. I. La radiographie des formations intrarachidiennes. p. 211. Edité par H. Fischgold et A. Wackenheim. Masson. Paris 1965
14. GREENFIELD J. G. Neuropathology. First edition. p. 29. E. Arnold. London 1960
15. HARVAY J. P. FREIERBERGER R. F. and WAXNER G. Clinical and experimental observations with methiodal an absorbable myelographic contrast agent. Clin. Pharmacol. Ther. 2 (1961) 610
16. HEDGECOCK J. und ZEITLER E. Histologische Veränderungen bei Myelographie mit positiven Kontrastmitteln. Radiologie 5 (1965) 508
17. HOWLAND W. J. and CURRY J. L. Experimental studies of pantopaque arachnoiditis. Radiology 87 (1966) 255
18. IMBELLANI L. et CHIGLIARINI J. M. Arachnoidite adhésive intrarachidienne à la suite de myélographies à l'éthiodane (pantopaque). J. Radiol. Électrol 52 (1971) 31
19. LEPOTTE LEBARD G. HEITE F. et LAURENT Y. M. Incidents et accidents en myélographie. I. La radiographie des formations intrarachidiennes. p. 203. Edité par H. Fischgold et A. Wackenheim. Masson. Paris 1965
20. LIVINGSTON K. Complications of myelography by alcohol. Acta radiol. 28 (1947) 69
21. MARON M. S. and RAAB J. Complications of pantopaque myelography. J. Neurosurg. 19 (1962) 302

- 22 MAYNIE W E DANIEL E F and ALLEN B M Acute meningeal reaction following pantopaque myelography J Neurosurg 34 (1971) 396
- 23 MONROE D Lumbar and sacral compression radiculitis New Engl J Med 254 (1956) 243
- 24 PEACHER W G and ROBERTSON R C L Pantopaque myelography. Results comparison of contrast media and spinal fluid reaction J Neurosurg 2 (1945) 220
- 25 PEPPER H und KLOKE H Über die Grundlagen einer Myelographie Arch klin Chir 134 (1925) 303
- 26 SCHÖNER R Röntgenkontrastmittel und Liquorraum Springer Berlin Göttingen Heidelberg 1964
- 27 SEHGAL A D GARDNER W J and DORN D F Pantopaque arachnoiditis Clin clin Quart 29-30 (1962-63) 177
- 28 SODERBERG L SJÖBERG S and LARSSON P Neurological complications following myelography with water soluble contrast media Acta orthop scand 28 (1958-59) 220
- 29 SIE MEYER W Histopathologie des Nervensystems First edition p 59 Verlag von Julius Springer Berlin 1922
- 30 TAREN J A Unusual complication following pantopaque myelography J Neurosurg 17 (1960) 323
- 31 WORMNER E BAUMGARTNER J et BRAUN J P Le diagnostic de la hernie discale lombosacrée par la myélographie au mono-sodo-méthane sulfonate de sodium Presse méd 63 (1953) 1584

SIDE EFFECTS OF WATER SOLUBLE CONTRAST MEDIA IN LUMBAR MYELOGRAPHY

L. IRSTAM

Water soluble contrast media of the Abrodil group have been used in Scandinavia for some thirty years. These have an irritating effect on the medulla and the nerve roots and cannot be used without spinal anaesthesia which is however not inert and adds to the toxic effect (GONSETTE 1971). Most of the complications of lumbar myelography are well known and have been dealt with in the comprehensive investigation of AHLÖREN & PRÄSTHOLM (1969) in which the frequency of side effects was stated to be more than 60 per cent.

Many attempts have been made to develop less irritating contrast media and have now and then been accepted with enthusiasm until later experience has proved them to have serious side effects. This occurred for example with SH 617 (Schering) first described as a long desired newcomer (ZETTLER 1965) but later considered unacceptable (FISCHER 1965 LUNDQVIST & TORNELL 1969). CAMPBELL *et al.* (1964) investigated the isothalamate compounds for their toxicity when injected intracisternally in animals. An increasing number of publications have since reported the use of isothalamate meglumine for lumbar myelography in man. The irritating effect of this contrast medium — Conray 60 — on the medulla and spinal roots is so slight that its use in myelography requires no spinal anaesthesia. The frequency of complications has been described as low although all the series published contain cases with complicating clonic convulsions or muscular fibrillations.

- 22 MAYNIE W. E., DANIEL E. F. and ALLEN B. M. Acute meningeal reaction following pantopaque myelography. *J Neurosurg* 34 (1971) 996
- 23 MONROE D. Lumbar and sacral compression radiculitis. *New Engl J Med* 254 (1956) 243
- 24 PEACHER W. G. and ROBERTSON R. C. L. Pantopaque myelography. Results comparison of contrast media and spinal fluid reaction. *J Neurosurg* 2 (1945) 220
- 25 PEPPER H. und KLOSS H. Über die Grundlagen einer Myelographie. *Arch. klin. Chir.* 134 (1925) 303
- 26 SCHÖNER R. Röntgenkontrastmittel und Liquorraum. Springer, Berlin-Göttingen-Heidelberg 1964
- 27 SEXTAL A. D., CAPONE W. J. and DOWD D. F. Pantopaque 'arachnoiditis'. *Cleveland Clin. Quart.* 29-30 (1962-63) 177
- 28 SODERBERG L., SJÖBERG S. and LANGELOF P. Neurological complications following myelography with water soluble contrast media. *Acta orthop. scand.* 28 (1958-59) 220
- 29 STEINMEYER W. Histopathologie des Nervensystems. First edition p. 59. Verlag von Julius Springer, Berlin 1922
- 30 TAREN J. A. Unusual complication following pantopaque myelography. *J Neurosurg* 17 (1960) 323
- 31 WORMS E., BALMONTIER J. et BRULM J. P. Le diagnostic de la hernie discale lombaire par la myélographie au mono iodo-méthane sulfonate de sodium. *Presse méd.* 63 (1955) 1581

Tabl 1

Frequency of side effects as reported in the literature (From Conarty 1971)

Authors	No of cases	Shock	Epilepsy	Paraplegia Cauda equina syndrome	Deaths
MONROE (1956)	121	—	—	10	—
LINDERLOM (1947)	721	32	—	3	—
SPÖCKENBERG (1959)	760	—	—	3	—
LEVERSETZ (1964)	800	—	2	4	—
COSTE (1961)	700	—	—	13	—
BUTTARD (1963)		—	—	7	—
Quoted by ECKOFFER (1960)			numerous		

throughout. In the Conray 60 patients 2 to 4 ml spinal fluid were aspirated and carefully mixed with 5 ml contrast medium, the mixture then being injected slowly for at least one minute. If the volume of medium mixture proved insufficient, which occasionally happened in patients with a wide subarachnoid space, a further 1 to 2 ml undiluted contrast medium were injected.

The first 200 patients examined with Dimer X were given equal volumes of spinal fluid and contrast medium. Eight to 10 ml of this mixture were injected, i.e. up to 5 ml medium. In 2 cases in which the subarachnoid space was wide a further 2 ml medium were injected, i.e. 7 ml undiluted Dimer X, in all. After these first 200 examinations the medium was diluted, i.e. the mixture consisting of 5 ml Dimer X mixed with 2 ml spinal fluid.

The patient was placed at an angle of about 15° in the lateral position with the head elevated, the beam horizontal and the spine bent forward to a varying extent, both sides being examined on one and the same occasion. Lateral views were obtained with the patient prone. The second half of the Conray 60 group and the entire Dimer X group patients were also examined standing with and without bending to the side. The course of the examination was followed by TV fluoroscopy or aural roentgenograms in all patients examined with Conray 60 or Dimer X as an aid in the prevention of the passage of the contrast medium up into contact with the medullary cone, i.e. not higher than to the lower margin of the first lumbar vertebra.

All the patients examined with Kontrast U were afterwards arranged supine with the trunk and the head slightly elevated for 4 to 6 hours, after which they lay flat for a further 18 hours. Those examined with Conray 60 were placed with the trunk and the head raised about 45° but those with Dimer X at about 30°.

Table 2
Frequency and types of side effects

	Kontrast U		Kontrast 60		Dimer X	
No. of myelographies	150		152		300	
No. of patients with side effects	85 57		39 26		86 28.3 %	
Hypereccitation signs	1 0.7		6 4			
Epileptic convulsions	1 0.7		0		0	
Clonic convulsions or muscle fibrillations	0		6 4		7 2.3	
Radicular signs	43 28		6 4		17 5.7	
Hyperalgesia esp. in the back	37 24		4 3		10 3.3	
Retention of urine	4 3		2 1		5 1.7	
Pain in the abdomen	1		0		2 0.7	
Meningeal irritation	77 51		36 23.7		86 28.3	
Cephalgia	16 11		21 14		53 17.7	
Nausea	16 11		3 2		16 5.3	
Rise in temperature no signs of meningitis	5 3		1 0.7		6 2.0	
Meningitis	0		0		1 0.3	
Fall in blood pressure total	40 26		11 7		10 3.3	
Fall in blood pressure with shock	6 4		0		1 0.3	

for 6 to 8 hours. The patients were then placed horizontal for a further 18 hours. All three groups spent at least 6 hours in the intensive care unit after conclusion of the examination.

Side effects during and after myelography performed with different water soluble contrast media fell essentially into three groups depending on the part of the nervous system irritated by the contrast medium or spinal anaesthetic.

The borderline between the different groups are to some extent fictitious. To the group meningeal irritation were assigned headache and hypotension, even though the site of the attack causing these disorders is unknown. Nausea or vomiting was also ascribed to this group. Signs of radicular involvement included hyperalgesia, by which is understood increased pain in the lumbar spine, possibly radiating in the legs. A few cases of neck pain without positive neurologic signs or evidence of meningitis were, however, also assigned to this group.

The division of the side effects of myelography with Kontrast U into two groups, i.e. those produced by the anaesthetic and those by the contrast medium was considered unrealistic: all the effects were therefore ascribed to the method as a whole. Side effects were observed in 55 per cent of the patients examined with Kontrast U. The most common effect of this type of examination was a fall in blood pressure which was recorded in 26 per cent of the patients including

4 per cent who went into a state of shock. The next commonest side effect (24 per cent) was hyperalgesia in the back. In the material examined with Conray 60 and Dimer X the commonest effect was headache (14 and 18 per cent respectively). Clonic convulsions or fibrillations in the legs occurred in 4 and 2 per cent of patients respectively. That part of the Conray 60 series premedicated with diazepam included a patient with mild clonic convulsions which were however soon controlled by diazepam intravenously. Clonic convulsions arose in 5 patients examined with Conray 60 without premedication with diazepam.

Discussion

The frequency of side effects of Kontrast U was judged from the hospital records of patients who had not been closely observed for even minor side effects. It may therefore be assumed that in the Kontrast U series minor effects, such as mild headache, nausea or headache had not been recorded.

Dimer X mixed with an equal volume of spinal fluid occasionally failed to produce satisfactory definition especially in patients with a wide subarachnoid space. A change of the ratio of the mixture of contrast medium and spinal fluid from 1:1 to 5:2 restored this defect. The frequency of side effects in those patients of the Dimer X series who received a mixture of contrast medium and spinal fluid in the ratio of 1:1 failed to differ statistically from that in those who received it in the ratio 5:2.

Contrast medium relatively low viscosity is useful for demonstrating changes in the filling of root pockets. Low viscosity medium will however rapidly collect in the most declive parts of the subarachnoid space when the patients are examined standing. Dimer X is somewhat more viscous than Conray 60, the former thus seemed to be more suitable for lumbar myelography than Conray 60 especially since nearly all patients were examined lying as well as standing.

The most serious complications of Conray 60 and Dimer X myelography and one that occurred in all published series were clonic convulsions or muscular fibrillations in the legs. The convulsions started 2 to 3 hours and never later than 4 hours after the examination. Slight clonic convulsions in the Conray 60 series however occurred in 2 patients as early as 20 to 30 minutes after the injection of the contrast medium. Two of the patients examined with Conray 60 had severe and prolonged convulsions recurring at various intervals of up to 24 hours despite repeated intravenous administration of diazepam. In the other patient with convulsions after Conray 60 the cramps were mild and were quickly controlled by diazepam.

Seven of the patients examined with Dimer X had convulsions, which were slight in 6 and soon controlled by diazepam. The seventh patient suddenly lost consciousness for a few seconds with a simultaneous marked fall in blood pressure two hours after the examination; this complication was promptly controlled but at the same time prolonged severe clonic convulsions confined to the left hip arose and despite intense and heavy medication with diazepam persisted for 8 hours. The convulsions resulted in a medial fracture of the femoral neck; the tendon reflexes were hyperexcitable for a further 48 hours after the convulsions had ceased. The contrast medium in all the cases in which the convulsions had occurred had inadvertently passed too high up the spinal canal and come into contact with the medullary cone. No uniform explanation can be offered for this high flow. Some of the cases may be caused by the head-end not being raised sufficiently, some by injection of too large a volume of contrast medium into a narrow subarachnoid space. Other causes might have been scoliosis, for which the examiner had not made sufficient allowance on change of posture of the patient.

✓ In the Conray 60 series, however, there were at least 10 cases and in the Dimer X series 8 cases where the contrast medium had come into contact with the medullary cone without producing convulsions. Such cases have been described by AHLGREN (1969).

✓ Convulsions did not occur in any case when the level of the contrast medium had not exceeded the lower border of L1. This corroborates the observation by AHLGREN (1969) and by GOMSETTE *et coll* (1968) that the frequency of convulsions is higher when the contrast medium is allowed to come into contact with the medullary cone.

After 200 examinations with Dimer X, personal experience as well as the literature suggested that more active prophylactic treatment of the patients after the examination might be employed. Those patients in whom the medium had apparently extended too high up the spinal canal were carefully observed for at least 12 hours in the intensive care unit. A second dose of 5 to 20 mg diazepam was injected intravenously as soon as possible, the dosage varying according to the patient's age, weight and bodybuild. The reflexes of the legs were continually checked; further doses of diazepam were administered if necessary. It is possible that repuncture and aspiration of spinal fluid may be useful as soon as it is noticed that the contrast medium has passed too far up the spinal canal so that as much as possible may be removed and further exposure of the medulla to injury avoided. The patient who had severe convulsions and fracture of the femoral neck had unfortunately not been treated in this way. No convulsions or fibrillations were observed in any of the other patients in the present material or in cases since examined.

GONSETT (1971) has reported that the earliest sign of incipient convulsions elicited by Conray 60 or Dimer X in man is the appearance of spikes in the EEG recordings made 1 to 3 hours after the end of the examination. All patients in whom the medium had risen too far up the spinal canal now have an EEG examination. No spikes have been observed probably because such activity is suppressed by premedication with diazepam.

AHLOREN (1971) reported clonic convulsions or muscular fibrillations in 4.8 per cent of 454 examinations with Conray 60 and in 3.8 per cent of 394 examinations with Dimer X. In a heterogeneous French series compiled by BAUMGARTNER *et coll.* (1970) the frequency of convulsions with Conray 60 was reported as 3.4 and with Dimer X 1.1 per cent. LEHTINEN & SEPPANEN (1972) reported muscular rigidity and myelonia in 14 per cent of 56 patients examined with Conray 60 and in 5.5 per cent of 54 patients examined with Dimer X.

The patients in the series of AHLOREN were not premedicated with diazepam on the grounds that it might mask early stages of convulsions or muscular fibrillations in the legs and that the drug in his opinion had no demonstrable prophylactic effect on convulsions. In the present investigation, however, the frequency of convulsions after the use of diazepam indicates that both it and its metabolites produce a considerable prophylactic effect for a long time after a single injection.

Meningitis occurred after myelography with Dimer X in one patient. Four hours after the examination the temperature rose to 39.3 with headache and increasing cervical rigidity but no focal neurologic signs. Twelve hours after the examination the CSF was highly cellular with preponderance of well preserved neutrophil leukocytes, a few lymphocytes and reticuloendothelial cells but no eosinophils. The appearances were compatible with a diagnosis of chemical meningitis. All symptoms disappeared within 3 days. The aseptic pathogenesis appeared to be established. Whether this aseptic meningitis was caused by the contrast medium or by lumbar puncture *per se* could not be decided. Such instances of chemical meningitis have been observed though rarely in association with encephalography.

In only a few cases of the Conray 60 series was the spinal fluid analysed 1 to 3 days after myelography. The spinal fluid of 12 patients was analysed 2 to 3 days after the examination in the Dimer X material. No changes were evident that could be related to the administration of the contrast medium with certainty.

The resorption time of the medium was determined in 4 cases in the Conray 60 and Dimer X series. Roentgenograms were obtained up to 12 hours following the examination and in no instance did these reveal contrast medium in the spinal canal later than 6 hours from the end of the examination. This is not in line with the finding by BRARANT *et coll.* (1971) that residual Dimer X may

be demonstrated in the spinal canal 8 to 9 hours after the examination

The advantage that a patient may be examined for a longer time with Conray 60 or Dimer X than with Kontrast U must be weighed against the disadvantage that these media are absorbed from the spinal canal much slower than the latter. This means that the patient must lie with the head-end of the bed raised for 4 to 6 hours after myelography with Conray 60 or Dimer X but almost flat after Kontrast U. The leakage of CSF is probably greater in the raised than in the horizontal position; this might at least partly explain the headache that occurred in all three series.

The high frequency of pain after myelography with Kontrast U is remarkable. The pain was severe and appeared 3 to 4 hours after the examination, i.e. when the spinal anaesthesia had worn off. This frequency was much higher than in the Conray 60 and Dimer X series in which the pain occurred at the end of the injection of the contrast medium and disappeared as soon as 1 to 2 ml had been aspirated from the spinal canal. Pain before the examination did not usually prevent the examination or the intensive care following the examination with Conray 60 or Dimer X. Diazepam in the main had a considerable palliative effect and only exceptionally were analgetics necessary.

The examinations performed with Conray 60 or Dimer X were generally easier throughout and the patients better to manage. The blood pressure was said to have fallen if the systolic reading had decreased by more than 30 mm; less fall was occasionally noted in all three series but was not enough to be recorded as a side effect of myelography. The fall in blood pressure following myelography with Kontrast U produced the largest group of side effects. Four per cent of the patients developed shock with a marked fall in blood pressure; these cases were difficult to manage and required prolonged attention. The contrasts with the fall in blood pressure recorded after Conray 60 or Dimer X in which it was generally slight and the patients were hardly affected. The blood pressure was rapidly restored to normal by raising the legs for a short time.

The time of onset of the fall in blood pressure differed in patients examined with spinal anaesthesia and Kontrast U on the one and patients examined with Conray 60 or Dimer X on the other hand. The fall in blood pressure after Kontrast U myelography was usually noted 30 to 45 minutes after the examination. Only in a small number of these patients did a fall in blood pressure occur up to 4 to 5 hours after the end of the examination. After myelography with Conray 60 or Dimer X the blood pressure usually decreased at 2 to 4 hours after the examination. The blood pressure never fell later than 6 hours after Conray 60 or Dimer X. These differences were probably due to differences in the rate of absorption of the three contrast media. It is also possible that the degree of leakage of the CSF after puncture caused by the position of the

patient in the three groups had some effect. The underlying mechanism of the fall in pressure is not known.

The occurrence of adhesive arachnoiditis after lumbar myelography with water soluble contrast media will be the subject of a forthcoming paper.

Conclusions

Since Dimer X is otherwise an excellent contrast medium for lumbar myelography owing to its high iodine content and its rate of absorption and since its irritative effect is so slight that the examinations may be performed without lumbar anaesthesia this medium appears to be the most suitable available for lumbar myelography. However careful observation of the patient after lumbar myelography, preferably in an intensive care unit and by specially trained personnel must be emphasized.

The other side effects occasionally occurring after Conray 60 and Dimer X suggest a low toxicity. The most serious effect of the use of Dimer X for lumbar myelography is the tendency to clonic convulsions or muscular twitchings in the legs. This is however uncommon and less frequent than after Conray 60. It also appears possible that the frequency and severity of convulsions may be reduced by the prophylactic medication with diazepam.

It is true that Kontrast U never produced convulsions thanks to spinal anaesthesia but otherwise caused side effects fairly often.

SUMMARY

Three contrast media Kontrast U, Conray 60 and Dimer X were compared as to the frequency of their side effects in similar series. Kontrast U produced such effects twice as often as Dimer X or Conray 60. The most serious side effects of the latter two contrast media were clonic convulsions or fibrillations in the legs, this being less common after Dimer X than after Conray 60. The high iodine content, suitable rate of absorption and relatively low toxicity suggest that Dimer X is preferable.

ZUSAMMENFASSUNG

Drei Kontrastmittel Kontrast U, Conray 60 und Dimer X, wurden hinsichtlich ihrer Häufigkeit von Nebenwirkungen in ähnlichen Serien verglichen. Kontrast U verursacht derartige Nebenwirkungen, deren schwere ereignisstechnische Krampf oder Fibrillationen der Beine, dreimal so häufig wie die anderen Mittel, obwohl solche häufiger nach Dimer X als nach Conray 60 auftraten. Der hohe Jodgehalt, die geeignete Absorptionseigenschaft und die relativ niedrige Toxizität lassen Dimer X als am besten geeignet erscheinen.

RÉSUMÉ

L'auteur a comparé sur des séries similaires les effets secondaires de trois moyens de contraste: Contrast U, Conray 60 et Dimer X. Le Contrast U entraîne de tels effets deux fois plus souvent que le Dimer X ou le Conray 60. Les effets secondaires les plus sérieux de ces deux derniers moyens de contraste sont les convulsions cloniques ou les fibrillations dans les membres inférieurs qui sont moins fréquentes après le Dimer X qu'après le Conray 60. Sa haute teneur en iode, sa rapidité d'absorption favorable et sa toxicité relativement basse font penser que le Dimer X est préférable.

REFERENCES

- ANLUNDEN P. Lumbale Myelographie mit Conray Meglumum 282. Fortschr. Röntgenstr. 111 (1969) 270
- Lumbal myelografi med Conray Meglumum 282 og Dimer X. (In Danish) Paper read at the meeting of the Nordic Society of Medical Radiology Reykjavik Jun. 1971
- og PRAESTHOLM J. Komplikationer ved myelografi med methiodalum. (In Danish) Nord Med. 92 (1969) 1600
- BAUMGARTNER J., BRAUN J. P., CARON J., CESTLE J., FICHTHOLD H., GORETTE R., HINCH J. F., LEGRE J. et METZGER J. Radioculographie au Dimer X. Premiers résultats après 630 examens. J. Radiol. Électrol. 51 (1970) 5,7
- BRANDT H., WEDDER H., GROTH W., KOSTADINOW G., CLEGGOWELL J. und LERNER H. D. Klinische Prüfung eines neuen wasserlöslichen Kontrastmittels zur lumbale Myelographie. Fortschr. Röntgenstr. 115 (1971) 609
- CAMPBELL R. L., CAMPBELL J. A., HEIMBURGER R. F. et coll. Ventricleulography and myelography with absorbable radiopaque medium. Radiology 82 (1964) 286
- FISCHER L. R. An experimental evaluation of pantopaque and other recently developed myelographic contrast media. Radiology 85 (1965) 537
- GORETTE R. An experimental and clinical assessment of water soluble contrast medium in neuroradiology. A new medium—Dimer X. Clin. Radiol. 22 (1971) 44
- et ANDRÉ BALZAUX G. Nouvelle technique de radioculographie lombosacrée par produit hydrosoluble résorbable sans rachianesthésie. Ann. Radiol. 11 (1968) 141
- LEHTINEN F. and SEPANEN S. Side effects of Conray Meglumum 282 and Dimer X in lumbar myelography. Acta radiol. Diagnost. 12 (1972) 12
- LINDORF E. and TOWELL G. Experiences with SH 617 L. Acta radiol. Diagnost. 9 (1968) 701
- ZATTEL E. Premiers résultats d'un nouveau moyen de contraste résorbable en myélographie. In: La radiographie des formations intrarachidiennes p. 167. Edited by H. Fischgold and A. Wackenheim. Masson & Cie Paris 1965.

FALSE CORTICAL ANEURYSM IN SUBDURAL HAEMATOMA FOLLOWING HEAD INJURY WITHOUT FRACTURE

K. BERGSTRÖM and A. HEMMINGSSON

Subdural haematomas following cranial injuries are usually caused by haemorrhage from convexity veins lying close to the large venous sinuses. Post-traumatic arterial subdural haematomas, on the other hand, are uncommon. DRAKE (1961) reported however that in a material of 100 cases with a subdural haematoma the bleeding was arterial in 11 cases following a lesion of a superficial cortical artery. A somewhat lower frequency was given by VANCE (1950) who stated that 6 of 102 subdural haematomas were due to arterial haemorrhage from cortical arteries; the cause of these subdural haemorrhages was discovered at operation. This arterial trauma may give rise to a false aneurysm; the origin of the subdural haemorrhage may then be determined preoperatively by angiography.

Cortical aneurysms, occurring after injury to the skull without fracture and producing subdural haematomas diagnosed preoperatively by angiography have been described by BASSETT & LEMMEN (1952) (one case), HIRSCH *et coll* (1962) (2 cases), SMITH & KEMPE (1970) (one case) and RUMBAUGH *et coll* (1970) (2 cases). SADIA *et coll* (1963) have described a case of subdural haematoma caused by rupture of a cortical aneurysm of a peripheral branch.

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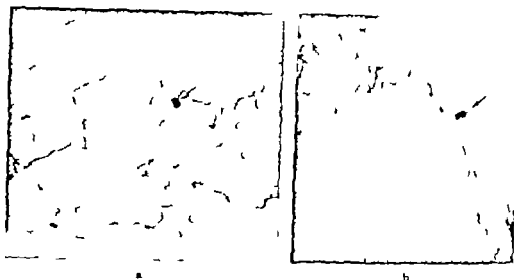


Fig. 1. Case 1. Left carotid angiography. a) Lateral b) a.p. projection. A subdural haematoma lies over the left hemisphere and an aneurysm the size of a grain of rice on a different artery within the former.

of the middle cerebral artery following head injury although they considered the aneurysm to be congenital. Two similar cases but with no preceding head injury have been reported by Boop et coll (1961) and Rumbaugh et coll (1970). False cortical aneurysms have been described by Go et coll (1971) among others in cases of subdural haematoma associated with lacerating fractures of the skull.

Two further cases of subdural haematoma caused by arterial haemorrhage following a closed head injury will now be reported. The origin of the haematoma in these patients was established angiographically before operation by demonstration of a cortical aneurysm.

Case reports

Case 1. A 47-year-old man sustained a closed injury to the left parietal region (hit by a falling tree) but did not lose consciousness. On the following day he had acute headache and vomiting but no fracture of the skull. Lumbar puncture: RBC 17 400 per ml cerebrospinal fluid; he was therefore considered at first to have a subarachnoid haemorrhage.

Left carotid angiography four days after the injury revealed a subdural haematoma 1.5 cm wide in the parietal region. Within the haematoma was an aneurysm the size of a grain of rice together with the afferent artery of a small peripheral branch of the middle cerebral artery (Fig. 1). The pericallosal artery and the internal cerebral vein were displaced 0.5



Fig. 2 Case 2 Left carotid angiography: a) Lateral b) β projection. A subdural haematoma lies over the left hemisphere with a pea-sized aneurysm and its afferent artery within the former.

cm to the right. Operation was performed the day after the angiography. The haematoma was evacuated in a parietal bone flap and the aneurysm within the haematoma resected. It proved to be a false aneurysm.

Case 2 A 64-year-old man sustained closed head injury in a car accident after which he developed progressively increasing headache, nausea, some loss of consciousness and weakness of the right side of the body. The skull was not fractured. Lumbar puncture was not performed. Twenty days after the injury left carotid angiography revealed a haematoma 2.5 cm wide in the frontoparietal area within this lay a pea-sized aneurysm together with the afferent artery of a small peripheral branch of the middle cerebral artery (Fig. 2). The pericallosal artery and the internal cerebral vein were displaced 2 cm to the right. Operation was performed 10 days after the angiography. The haematoma was evacuated in a parietal bone flap and the aneurysm within the haematoma was excised. It was a false aneurysm.

Discussion

These two cases of subdural haematoma combined with a cortical arterial aneurysm as those described in the literature had a course not different from that of a subdural haematoma of venous origin.

According to Boop et al. (1961) one to two per cent of all subdural haematomas are caused by a congenital aneurysm which owing to a subdural site or to a lesion in the arachnoid give rise to haemorrhage into the subdural

space. These congenital aneurysms are usually localized to the basal cerebral arteries, while the false cortical aneurysms lie on small peripheral branches of the middle cerebral artery. This situation indicates that these cortical aneurysms are acquired, which is supported by the histologic findings.

Leptomeningeal arterial anastomoses have been described by VAHCF (1950) MOUNT & TAVERAS (1957) WEIDNER et coll. (1965) and HAWKINS (1966) among others. The cortical aneurysms now reported certainly developed on such an artery as it passed through the subdural space, within which the aneurysm and its feeding artery lay within the haematoma. An explanation for the development of the aneurysm may be that the artery from which it had arisen passed through the arachnoid membrane to the dura mater. Displacement of the membranes by head injury could therefore have led to erosion of the vessel with laceration of its wall, rendering possible the formation of a false aneurysm. Red blood cells in the cerebrospinal fluid in Case 1 and in two of the cases reported in the literature suggest that a lesion in the arachnoid membrane had also occurred.

SUMMARY

Two cases in which a false aneurysm was evident within a subdural haematoma following a closed head injury are described. The aneurysm probably developed through damage to leptomeningeal anastomoses and was therefore caused by arterial haemorrhage.

ZUSAMMENFASSUNG

Zwei Fälle bei denen ein Aneurysma spurium innerhalb eines subduralen Hämatoms nach einem geschlossenen Schädeltrauma nachweisbar war werden beschrieben. Die Aneurysmen hatten sich wahrscheinlich infolge einer Schädigung der leptomeningealen Anastomosen entwickelt und sind deshalb durch eine arterielle Blutung hervorgerufen.

RÉSUMÉ

Présentation de deux cas où il y avait un faux anévrisme dans un hématome sous-dural à la suite d'un traumatisme crânien fermé. L'anévrisme s'était probablement développé par lésion des anastomoses lepto-méningées et était donc causé par une hémorragie artérielle.

REFERENCES

- BASSETT R. C. and LEVICKI J. J. Subdural hematoma associated with bilateral intracranial aneurysm. *J. Neurosurg.* 9 (1952) 443.
BOOR L. W. C., CARU S. N. and FURNESS L. A. Ruptured intracranial aneurysm complicated by subdural hematoma. *J. Neurosurg.* 18 (1961) 834.

- DRAKE C G Subdural haematoma from arterial rupture J Neurosurg 18 (1961) 597
- GO K G, PERNICELLI L and OREN T S Acute subdural haematoma in connection with angiographically demonstrated traumatic rupture of cortical cerebral artery (presenting as false aneurysm) Neuroradiology 2 (1971) 107
- HAWKINS T D The collateral anastomoses in cerebro-vascular occlusion Clin Radiol 17 (1966) 203
- HUBCH J F, D'VIA M et SACCHIS M Les anévrysmes artériels traumatiques intracrâniens Neuro-chirurgie 8 (1962) 189
- MOUNT L A and TAYLOR J M Arteriographic demonstration of the collateral circulation of the cerebral hemispheres Arch Neurol Psychiat 78 (1957) 235
- REINBERGH C L, BURGEROT R T, TALLALLA A and KURZE T Traumatic aneurysms of the cortical cerebral arteries Radiology 96 (1970) 49
- SADIK A R, ADACHI M and RABENOWITZ J Rupture of an intracranial aneurysm within the subdural space—in association with trauma J Neurosurg 20 (1963) 609
- SADIK D R and KURZE L G Cerebral false aneurysm formation in closed head trauma J Neurosurg 32 (1970) 357
- VANCE B M Ruptures of surface blood vessels on cerebral hemispheres as cause of subdural hemorrhage Arch Surg 61 (1950) 997
- WEINBER W, HANAYEK W and MARSHAM CH Intracranial collateral circulation in leptomeningeal and rete mirabile anastomoses Neurology 15 (1965) 39

ISOLATED FRACTURE OF THE BASE OF THE SKULL WITHIN THE SELLA REGION

G O CARLSON M HAZELING and C MOLIN

The mechanism of fractures within the facial skeleton is usually evident. This may however occasionally be complex and only meticulous examination may disclose the full extent of the injury. The conditions arising in the facial skeleton in traffic accidents have been investigated in model experiments (HUELAR & HARGREY 1969).

A blow on the mandible usually does not produce a fracture of the anterior cranial fossa although fractures of the articular fossa of the mandibular joint may sometimes occur (WHITAKER 1966, PEROX & MERRILL 1970). The probable reason for this extremely rare consequence of a blow on the mandible is the ease with which fractures occur through the collar of this bone absorbing the force of violence.

An isolated fracture of the base of the skull within the central part of the sphenoid bone with displacement of the sella turcica region might presumably be caused either by a penetrating blow to this region or by a tangential stroke to dislocate the lower jaw so that one of the rami struck the area immediately below the sphenoidal sinus.

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Fig. 1 Horizontal lateral projection and lateral tomogram of the sella turcica. Air in both cisterns and on the convexity of the brain. Fracture through the sella turcica and chiasm with cranioposterior rotation of the body of the former.

Case report

A girl aged 17 was admitted after a traffic accident. In addition to fractures of hand and ankle she had fractures of the mandible, maxilla and base of the skull. Films of the head revealed air in the lateral cisterns and on the convexity of the brain (Fig. 1), leakage of cerebrospinal fluid was also evident. According to the record the patient had not lost consciousness and she herself stated that she had had a blow on the lower jaw and the lower part of the right upper jaw. Emergency examinations revealed inter alia bilateral fractures through the right mandibular condyle, comminuted fracture of the anterior part of the mandible with displacement, fracture of the trigonum mentale and comminuted fracture of the anterior part of the right maxilla involving mainly the alveolar processes and the front teeth. Supplementary examinations including tomography of the facial skeleton and skull base disclosed a splintered fracture involving the sphenoidal sinus and the region of the sella turcica. The fracture ran through the right half of the sphenoidal sinus extended into the lesser sphenoid to the sphenoparietal suture and chiasmatic sulcus to produce slight tilting and displacement of the fragments (Fig. 2). The fracture below the sella turcica caused the fragment of its body to be slightly rotated and displaced dorsally. There was some suggestion of fracture involving the right temporal bone since blood was present in the cavity tympani in the acute stage but no lesion could be discovered on tomography, ear and lat. examinations.

The fractures of the mandible bilaterally involved the narrowest part of the necks. The articulating condylar fragment of the right mandible inclined medially at an angle of about 45 degrees and was displaced 2 cm or more in the same direction. The left condyle was displaced and was inclined laterally.

Following the lesion in the region of the sella turcica hypophyseal insufficiency, thyroid hypofunction, diabetes insipidus, limitation of the field of vision and temporary diplopia developed. Signs of mental retardation occurred probably caused by communicating



Fig. 2 Tomography (a) Fracture through sphenoidal sinus with slight displacement of fragments to the left (→) (b) Medially displaced head of right side of mandible (→)

hydrocephalus consequent on injury to the basal cisterns. Most of the symptoms and signs receded and some 18 months after the accident moderate diabetes insipidus and mild mental retardation remained.

The data collected mainly from roentgen examinations suggest that the injury to the anterior and middle cranial fossae arose as follows: (1) The patient was flung forwards so that her face struck the instrument panel of the car, the main force of the impact being directed obliquely from below to the right side of the mandible. The upholstery of the panel distributed the force widely over the face to produce excoriations and haematomas of the skin. (2) The mandible was fractured and displaced to the left (Fig. 3). (3) The upper part of the fragment of the right ramus met the body of the sphenoid bone slightly below the sphenoidal sinus and injured this area. The force of the impact was propagated to the sella turcica which was displaced. (4) When the pressure ceased the mandibular fragments resumed an almost normal position. The condyles lagged behind in this return movement and both therefore were displaced to the left (Fig. 3).

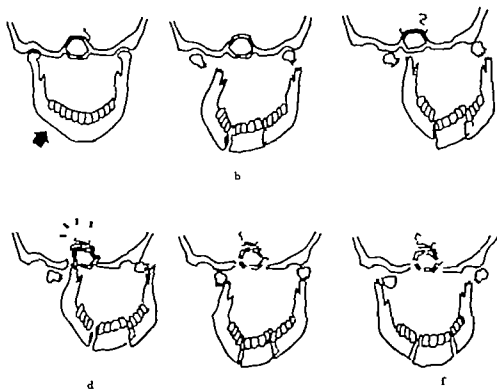


Fig 3 a) Blow to right side of the mandible b) fractures of anterior part of body and necks of mandible c) fragments markedly displaced to the left so that d) the upper part of the fragment of the right ramus struck the base of the skull at the sphenoidal sinus to produce fracture of the sella turcica e) The mandibular fragments spring back f) Position of the fragments in the acute stage

Discussion

No signs of penetration of the face or mouth were evident so that the isolated fracture in the region of the sella turcica can have arisen solely through the head of the right side of the mandible hitting this region from below right. With the fragmentation of the neck a considerable part of the force of impact was dissipated which is probably the reason why no deeper penetration occurred. Since the main direction of energy of the blow was tangential the mandible was displaced backwards and to the left. This probably resulted in further reduction of the force of impact but at the same time in injury to the central region of the base of the skull.

SUMMARY

A case of fracture of the sphenoid bone involving the sella turcica and the clivus following a blow on the mandible producing bilateral fractures of the necks is described. The mechanism of trauma is discussed.

ZUSAMMENFASSUNG

Der Fall einer Fraktur des Keilbeins mit Beteiligung der Sella turcica und des Clivus nach einem Schlag auf die Mandibel mit bilateraler Fraktur des Nackens wird beschrieben. Der Mechanismus eines Traumas wird diskutiert.

RÉSUMÉ

Présentation d'un cas de fracture du sphénoïde atteignant la selle turcique et le clivus après un coup sur la mandibule ayant entraîné des fractures bilatérales des cols des condyles. Les auteurs examinent le mécanisme du traumatisme du sphénoïde.

REFERENCES

- HULLER D F and HARGREY J H: Maxillofacial injuries: their nature and mechanisms of production. *J Oral Surg* 27 (1969) 451.
- PIROK D J and MERRILL R G: Dislocation of the mandibular condyle into the middle cranial fossa. *Oral Surg* 29 (1970) 15.
- WHITACRE W B: Dislocation of the mandibular condyle into the middle cranial fossa: Review of the literature and report of a case. *Plast reconstr Surg* 38 (1966) 23.

ROENTGENOGRAPHIC DEMONSTRATION OF THE EUSTACHIAN TUBE IN CHRONIC OTITIS MEDIA

ADELE FERBER and J. HOLMQUIST

General agreement exists concerning the important role of Eustachian tube dysfunction in the development and persistence of chronic otitis media in which it has often been demonstrated by the air pressure equalization technique (MILLER 1965 FLISBERG 1966 HOLMQUIST 1969). However controversy exists concerning the reason for the poor function in these cases and it was consequently felt that roentgenographic investigation might afford further information.

Anatomy. The anatomic connection between the middle ear and the nasopharynx via the Eustachian tube is osseous as well as cartilaginous. The osseous part consists of an extension of the middle ear cleft into which inflammation of the middle ear readily extends (SCHUKNECHT & KERR 1967). Pneumatised cells may sometimes surround this part of the tube. It is possible that tubal infection may persist in these cells for a long time in a manner similar to residual infection in the air cells of the mastoid. The cartilaginous part is only partly surrounded by cartilage and the mucosa is folded. Consequently the tube is collapsed at rest but opens on contraction of the tensor veli palatini muscle during swallowing and



Fig. 1. Position of the head in the fronto-oblique (a) and axial (b) projection for examining the right Eustachian tube.

yawning. The junction of the two parts, known as the isthmus, has a diameter of only 2 to 3 mm.

Method. The Eustachian tube was examined with Endografin (Schering) (N,N' -adipic di 3-amino-2,4,6-trisubstituted benzoic acid; viscosity 18 cps at 37°C) a water-soluble contrast medium that was well tolerated. A 500 ml bottle containing the contrast medium at 37°C was suspended 500 mm above the level of the external auditory canal to which it was connected by 4 mm plastic tubing. A seal was obtained in the external canal with a rubber olive. Two projections (Fig. 1) and at least two exposures were the rule in each position. The patient was instructed to swallow repeatedly during the examination but not during the exposure.

Material. Sixty-eight ears with chronic otitis media in 59 adults were examined. All ears had a dry tympanic membrane perforation and no signs of infection were evident in the otomicroscope. In 36 of the 68 ears Eustachian tube function was tested by the air pressure equalization technique (Flisberg et al. 1963). This test was performed before the examination.

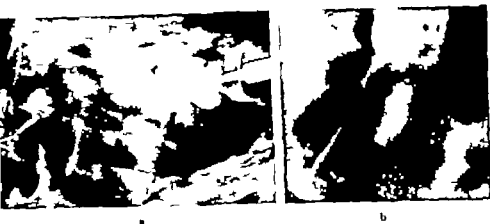


Fig 2 Patent tube. The contrast medium also appears in the nasopharynx. a) Frontal view b) Axial view

Results

The contrast medium appeared in 47 (70 per cent) of the 68 ears examined in the osseous as well as the cartilaginous part of the tube with traces in the nasopharynx (Table 1). This indicated a patent Eustachian tube (Fig 2). However 15 of the 47 ears presented signs of partial obstruction in the osseous part (Fig 3) while in 21 of the 68 ears (31 per cent) no contrast medium was evident in the cartilaginous part (Fig 4). A blockage could usually be seen in the osseous part but the medium was sometimes visible down to the isthmus without any roentgen changes being apparent.

Thirty six ears were tested by the air pressure equalization technique and only 13 proved to have completely normal Eustachian tube function (Table 2). The relationship between the roentgen findings and the tubal function tests appear in Table 2. Nine ears with normal findings at the roentgen examination all had normal tubal function. However in the group with partial blockage of the os

Table 1

Roentgen findings in 68 ears

	Number	Percentage
Patent tube	37	47
Partial blockage	15	22
Complete blockage	21	31

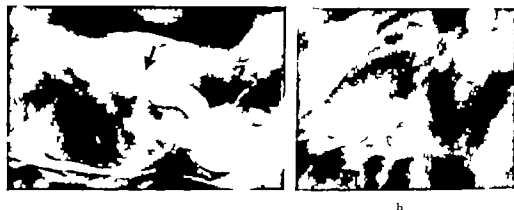


Fig. 3. Partial blockage of Eustachian tube in its osseous part (arrow). a) Fronto-oblique view b) Axial view.

seous part, only 4 had normal tubal function. In the group with roentgenologic blockage of the tube 14 out of 16 ears had poor tubal function while in the remaining 2 cases tubal function was normal. The tube was not explored so that the reason for the discrepancy is not known.

Discussion

Techniques for investigation of the Eustachian tube have earlier been reported in the literature (WELIN 1947, COMPÈRE 1958, WRITENBORO & NEUMAUER 1963, KAHN 1967). The procedures have, however, not generally been accepted as clinical routines. The one now described differs from those previously published in that a continuous flow of contrast medium is employed which means that even its rapid passage into the pharynx will allow satisfactory delineation of the tube. Furthermore, no instrumentation is necessary to introduce medium into the tympanic cavity as in other reports (COMPÈRE 1958). The whole proce-

Tabl. 2
Relation between roentgen findings and Eustachian tube function

	N of ears	Poor function		Normal function	
		N		No	
Patent tube	9	0	0	9	100
Partial blockage	11	7	64	4	36
Complete blockage	16	14	88	2	12



Fig. 4. Blockage of tube. No contrast medium in the cartilaginous part nor in the nasopharynx.

ture may be performed in the roentgen department without assistance from the otologist. The demonstration of the osseous part of the Eustachian tube seems to be of special importance from the view point of middle ear surgery. Inflammatory changes in the middle ear easily spread to the mucosa of the bony tube. The osseous part in chronic otitis media may consequently be obstructed, the lumen being filled with polypoid mucosa, fibrous tissue and new bone (SCHUKNECHT & HERR 1967). Such changes may unfortunately be easily overlooked in a routine middle ear operation. A total of 36 of 68 ears (53 per cent) had abnormalities at roentgen examination. As 6 of the 15 ears with completely normal tubal function had blockage of the tube it was felt that the roentgen examination in these ears was a valuable complement to the tubal function test.

Surgery of the bony part of the tube is up to now seldom performed, although it is hoped that this may be developed.

The technique now presented appears to constitute a significant contribution to the adequate evaluation of the Eustachian tube and should be included in routine otomicroscopy, roentgenology of the mastoid and middle ear, audiometry and tubal function tests before surgical intervention in middle ear disease. Final assessment of the value of the method has to await the results of careful control investigations of the latter.

SUMMARY

A modified roentgenologic technique for contrast filling of the Eustachian tube has been used in 68 ears with chronic otitis media and perforated drums in 59 adults. The findings and the relationship to tubal function by means of an air pressure equalization technique are discussed.

ZUSAMMENFASSUNG

Eine modifizierte Technik für die Kontrastfüllung der Tuba Eustachii wurde zur Untersuchung von 68 Ohren bei 59 Patienten mit chronischer Otitis media und perforiertem Trommelfell verwendet. Die Ergebnisse in Relation zur Tubenfunktion geprüft mit der Druckausgleichstechnik werden diskutiert.

RÉSUMÉ

Description d'une technique radiologique modifiée pour remplir de moyen de contraste la trompe d'Eustache dans 68 oreilles atteintes d'otite chronique moyenne et de perforation du tympan chez 59 adultes. Les auteurs décrivent les signes radiologiques et leur relation avec la fonction tubaire grâce à une technique d'égalisation des pressions acoustiques.

REFERENCES

- COVERS W. E. Tympanic cavity clearance studies. *Trans. Amer. Acad. Ophthal. Otolaryng.* 62 (1958) 444.
- FLINBERG K. Ventilatory studies on the Eustachian tube. *Acta otolaryng.* (1966) Suppl. No. 219, p. 1.
- , BRUNELSTEDT S. and ÖRTENGREN U. Controlled ear aspiration of air. *Acta otolaryng.* (1963) Suppl. No. 182, p. 35.
- HOLMQUIST J. Eustachian tube function in patients with ear drum perforations following chronic otitis media. *Acta otolaryng.* 68 (1969) 391.
- KARR N. Röntgenologische Kontrastdarstellung der Ohrentrompete. *Hals, Nas. u. Ohren. Arzt* 75 (1967) 60.
- MILLER G. JR. Eustachian tubal function in normal and diseased ears. *Arch. Otolaryng.* 81 (1965) 41.
- SCHUMBERGER H. and KARR A. Pathology of the Eustachian tube. *Arch. Otolaryng.* 86 (1967) 497.
- WELLS S. On the radiological examination of the Eustachian tube in cases of chronic otitis. *Acta radiol.* 28 (1947) 95.
- WITTEMBERG M. H. and NEUBAUER B. D. Simple roentgenographic demonstration of the Eustachian tubes and abnormalities. *Arch. Otolaryng.* 89 (1963) 1194.

TOINOGRAPHIC EXAMINATION OF THE VERTICAL SEGMENT OF THE FACIAL CANAL

S ERICSON and B LILJEQVIST

The aetiology of idiopathic peripheral paresis (Bell's palsy) remains obscure in spite of comprehensive investigations. Most authorities believe however that the paresis is a consequence of vascular or inflammatory alterations in the facial nerve or adjacent tissues (KETTEL 1959, 1963, SADE *et coll.* 1965, BLATT & FREEMAN 1966, GIANCARLO & MARTUCCI 1970). The course of the nerve through a channel in the bone, the facial canal, has been considered to be the predisposing factor of the paresis because ischaemia resulting from vascular or inflammatory oedema leads to neurolysis. Since the condition is practically unknown elsewhere in the body the unique anatomy of the facial nerve may be the causal factor although no proof of this hypothesis has been adduced.

JENSEN (1965) and ZILATROFF PEDERSEN (1965) have demonstrated by neurophysiologic methods that the lesion in Bell's palsy usually involves the nerve trunk that lies within the lower part of the facial canal below the geniculate ganglion and in about half the cases below the origin of the chorda tympani, that is to say in the vertical segment of the canal. JONGAERTS (1965), MILLER (1967) and MAY (1970) have also reported that in most cases the lesion appears



Fig. 1. Lateral tomograms of temporal bone at intervals of 1 mm in medial direction demonstrating the sectioning technique. Section C was used for the measurements.

at the level of the tympanomastoid segment of the facial canal between the bend at the posterior end of the horizontal part and the stylomastoid foramen.

The gross anatomy of the vertical segment of the facial canal is in the main constant although individual deviations have been observed in its course, even in normal cases (KETTEL 1959, 1963; FOWLER 1961; MIEHLE 1965). This also applies to its length and width. On the other hand little is known of the extent to which these parameters vary possible anomalies within the canal lumen and their importance as predisposing factors in the development of idiopathic peripheral facial paresis. Against this background it has proved of interest to carry out a radiographic examination of the normal variability of the vertical segment of the facial canal. It was considered that the findings might serve as a basis for the appraisal of the anatomy in pathologic conditions such as Bell's palsy.

Material. Tomography was performed in 35 healthy subjects of both sexes aged from 21 to 40 years of the vertical segment of the canal for the facial nerve alternately on the right and left sides. The subjects were chosen at random from students who neither at the time of the examination nor previously had had facial paresis, chronic ear affections, skull fracture or any other condition that might produce permanent damage to the facial canal or adjacent organs. The vertical segment of the canal could not be clearly demonstrated or else no tomograms could be obtained of good enough quality for measurements of the dimensions of the canal in 5 subjects who were excluded. The final material thus comprised 30 patients, 13 of whom were women and 17 men.

Method. The vertical segment of the facial canal from the outer bend of the second elbow to the stylomastoid foramen was examined in a lateral projection

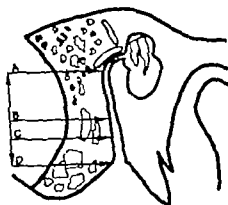


Fig. Tomographic cut through the vertical segment of the facial canal from the outer part of the second elbow to the stylomastoid foramen. Measurements performed at levels A, B, C and D.

by the method proposed by BRUNNER *et coll* (1963) BRUNNER & PADERSEN (1970) and HARRISON & BORROWS (1969). During the exposures the patient lay in the prone position with the head resting on the object table. The side of the head on which the examination was to be performed was turned upwards and oriented so that the sagittal plane was parallel to the table. The central ray was directed at the posterior border of the external auditory meatus; the enlargement factor due to the ray geometry was 1.3.

Because of the anatomic variations in the position of the facial canal in the temporal bone and as well as its narrowness a preliminary orientation of the depth of the tomographic section was performed. Five sections at intervals of 1 mm were made at distances of 2.6 and 3.1 cm from the skin anterior to the tragus sections and subsequently served as references for the real examination (Fig. 1). The films were taken with a Polytome tomograph (Masset Philip 0.6 mm focus FFD 130 cm) and hypocycloid movement.

Measurements. The tomogram in which the vertical segment of the facial canal was projected and in which the canal also appeared widest was used as a basis for the measurements. The contour of the canal was marked with a sharp pencil and measurements made of its length and of its width at the highest point.

A) at half the height (B) and at a point (C) located midway between B and the stylomastoid foramen. In addition the diameter of the lumen of the canal at the stylomastoid foramen (D) was measured (Fig. 2). This was performed to the nearest tenth of a millimetre with a magnifying glass by two independent investigators. They also estimated the occurrence of mastoid cells adjacent to the vertical segment of the canal, the number being graded as none (0), moderately numerous (1) and numerous (2).

Tabl 1

Means (\bar{x}) and standard deviation (SD) of the width of the facial canal (vertical segment) measured independently by two investigators (IN 1 IN 2) in lateral tomograms at levels A B C and D the length and the smallest width of the canal and the mean difference between the tallest gaters (\bar{d}) are indicated (mm)

	IN 1 $\bar{x} \pm SD$	IN 2 $\bar{x} \pm SD$	IN 1 minus IN 2 $\bar{d} \pm SD$	Significance (t test)
Width t A	1.9 \pm 0.40	1.9 \pm 0.43	-0.02 \pm 0.25	not significant
Width t B	2.1 \pm 0.40	2.0 \pm 0.45	0.11 \pm 0.31	not significant
Width t C	4. \pm 0.30	2.3 \pm 0.37	0.01 \pm 0.37	not significant
Width t D	3.7 \pm 1.29	3.8 \pm 1.24	-0.01 \pm 0.4	not significant
Smallest width	1.8 \pm 0.36	1.7 \pm 0.39	0.10 \pm 0.2	t = 2.16
Length	16.4 \pm 3.20	16.7 \pm 3.28	-0.23 \pm 0.68	not significant

Tabl 2

Coefficients of correlation between recorded values for the vertical segment of the facial canal at the levels A B C and D the length and the smallest width of the canal and the number of cells at the canal calculated in lateral tomograms by two independent investigators

A	B	C	D	Smallest width	Length	Cells
0.83	0.71	0.74	0.94	0.82	0.9	0.79

Tabl 3

Coefficients of correlation between the length and width of the vertical segment of the facial canal the sex and the presence of mastoid cells along the canal

	A	B	C	D	Smallest width	Length	Cells Sex
Width at A		0.61	0.35	0.31	0.9	0.27	0.02 -0.38
Width t B			0.77	0.39	0.74	0.04	0.03 -0.6
Width C				0.71	0.49	0.39	-0.07 -0.39
Width D					0.49	0.47	0.08 -0.38
Smallest width						0.35	0.07 -0.64
Length							0.31 -0.3
Cells							0.08

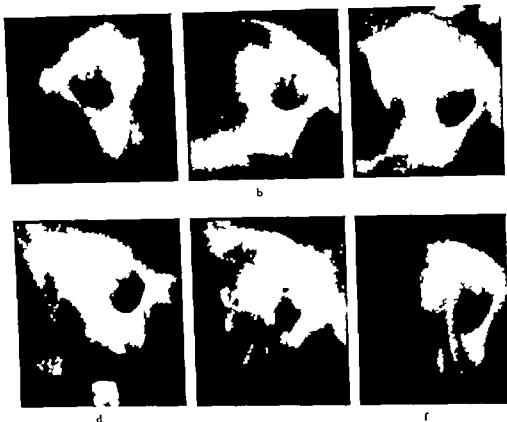


Fig 3 Tomograms of vertical segment of facial canal with variations in widths and lengths and various numbers of mastoid cells

The mean (\bar{x}) standard deviation (SD) and correlation coefficients (r) were calculated in accordance with the usual statistical rules by means of a computer. Analysis disclosed the distribution of the measured values to be approximately normal. The analysis of significance was performed by the t test for the measured values and by the γ test for the non-parametric values.

Results

The results are presented in Tables 1 to 4 and Figs 1 and 3. Table 1 gives the length of the vertical segment of the facial canal, its width at levels A, B and C and the smallest diameter of the lumen recorded empirically by two independent investigators; it also indicates the discrepancy between investigators for a single determination (\bar{d}) and the variation of the difference expressed as the standard

Table 4

Means (\bar{x}) and standard deviation (SD) of the vertical segment of the facial canal in lateral tomograms at the levels A, B, C and D. The length and smallest width of the canal for men and women (mm)

	N	A $\bar{x} \pm SD$	Signifi- cance (t test)	B $\bar{x} \pm SD$	Signifi- cance (t test)	C $\bar{x} \pm SD$	Signifi- cance (t test)
Men	17	2.1 \pm 0.37	t = 3.41	2.2 \pm 0.26	t = 3.72	2.5 \pm 0.31	t = 9.43
Women	13	1.6 \pm 0.40		1.8 \pm 0.36		2.1 \pm 0.58	
Range		1.2-2.6		1.0-2.6		1.1-3.3	

deviation of the recorded values. The differences between the observers were small and not significant. A χ^2 test was performed in respect of the presence of mastoid cells along the canal. The difference between the observers was again small and not significant.

An analysis of correlation in respect of the agreement between the investigators for a single observation disclosed high or extremely high coefficients for all factors examined (Table 2).

In 22 subjects (73 per cent) the smallest width of the canal occurred at A and in 5 (17 per cent) at B with a maximum difference A-B of 0.2 mm. In 3 subjects (10 per cent) the lumen was identical in A and B; the lumen widened steadily over its vertical course towards the stylomastoid foramen. This observation is confirmed by the high correlation coefficients for the relationship between closely located points. Between the length and width of the canal a positive but fairly low relationship was however recorded (Table 3); no correlation existed between the presence of mastoid cells and the length or width of the canal (Table 3).

The inter subject variation of the lumen width was fairly large (Table 4); it was approximately the same at the levels at A, B and C although the variability of the stylomastoid foramen and the canal length was greater owing to some extent to a few extreme values (Table 4).

Differences in the vertical segment assignable to sex were examined; the mean difference between the two investigators' registrations of each variable was tested and the correlation coefficients calculated (Tables 3, 4). All the reference points except those for the canal length were sex dependent with small values for the women. Significant mean differences were obtained for the canal width/lumen at levels A, B and C and for the smallest recorded width. The difference between the maximum and minimum value was however large. As regards the presence of mastoid cells along the canal there was no sex difference.

Table 4 (cont.)

D ±SD	Signifi- cance (t test)	Smallest width ±SD	Signifi- cance (t test)	Length ±SD	Signifi- cance (t test)
41 ± 1.7*	t = 1.90	1.20 ± 0.23	t = 4.37*	17.4 ± 2.4	t = 1.4
33 ± 1.10		1.5 ± 0.39		15.5 ± 4.24	
1.7-7.0		0.9-2.4		11.3-22.1	

Discussion

The vertical segment of the facial canal was clearly demonstrated in 87 per cent of the subjects and in these it ran parallel to the sagittal plane. The canal curved medially or was poorly defined owing to the presence of numerous mastoid cells in the cases in which the vertical segment of the canal could not be reproduced over its whole length in one tomogram. The depth of the section coincided with a demonstration of the ossicles (Figs 1-2) because these are readily identifiable they are highly suitable as reference points for detail planning of the section depth in tomography of the facial canal.

It is evident from the figures that the facial canal fails to follow a constant and strictly vertical course in the sagittal plane but often curves slightly in an anterior or posterior direction. Variations in the course of the canal have been reported earlier by, among others, KATTEL (1959) but seem from the literature to be fairly uncommon. The bending in the sagittal plane in this series was associated with the size of the mastoid process being less marked in subjects in whom this was large. From the anatomic course of the canal it would appear that the lateral projection is the most suitable one for tomographic demonstration of the mastoid portions of the facial nerve canal, a view that has also been expressed by HARRISON & BURROWS (1969) and BRUNYER & PEDERSEN (1970).

An examination of the tomographic appearances of the finer anatomic structures of the spinal column and temporal bone in the tomographic sections was performed by REICHMANN (1972 a, b) and ECKERDAL (1973). They employed the Polytome tomograph and hypocycloid movement and reported close agreement between the roentgenogram and the anatomy basis. The random selection of the subjects in the present investigation and the results as regards the demonstration of the vertical segment of the canal in the tomogram thus suggests that the values observed of the length and width of the canal are representative

of those for healthy adults in general. They might therefore serve for an appraisal of the canal in pathologic conditions.

The investigation was performed alternately on the right and left sides, one side per individual, in order to limit the dose. Since there were no left-right differences this can hardly have influenced the results.

The dimensions of the canal displayed large intersubject variation particularly in length, as well as in width at the stylomastoid foramen. These two anatomic variables were not associated with the width of the canal at any other level. However, it is possible that in a larger series the occasional extreme values would be less flat. The variation in width and length greatly exceeds the values reported in the sparse literature (JEPSEN 1965; BRUNNER & PEDERSEN 1970; Saito et coll. 1970). No corresponding investigation has, however, been performed.

The diameter of the upper and middle parts of the canal was on average less in the women, while the length and the width of the stylomastoid foramen presented no significant difference. Although they have not been noted in the literature before, the sex differences are plausible and may be ascribed to the general sex differences in the cranial dimensions (BERGQUIST 1957). It is possible that the sex differences observed in the canal may account for the overrepresentation of women with idiopathic facial paresthesia reported by POPE (1969) and ROBINSON & POE (1972); a closer investigation of this point is in progress.

SUMMARY

The normal variability in the vertical segment of the facial canal formed a basis for the appraisal of the canal in pathologic conditions and was investigated by lateral tomography in 35 healthy subjects of both sexes. Extremely great individual variations in the dimensions were evident, although these were less in the women than in the men.

ZUSAMMENFASSUNG

An 35 Individuen Männern und Frauen wurde die laterale Tomographie des Felsenbeins angewandt um den vertikalen Schenkel des Facialiskanals unter pathologischen Bedingungen mit der Norm vergleichen zu können. Es zeigte sich, dass diese Norm grossen Schwankungen unterworfen ist, obwohl bei Frauen weniger Schwankungen als bei den Männern beobachtet werden konnten.

RÉSUMÉ

La variabilité normale du segment vertical du canal du facial est la base de l'examen du canal dans les états pathologiques. Il a été étudié par tomographie de profil chez 35 sujets en bonne santé des deux sexes. Cette étude montre des variations individuelles extrêmement grandes dans les dimensions du canal, cependant ces variations sont moins importantes chez les femmes qu'chez les hommes.

REFERENCES

- BERGMANOFF W. Messungen von Winkeln und Strecken an Röntgenbildern des Schädels. Fortschritt Röntgenstr. 77 (1957) 62
- BLATT I. M. and FREEMAN J. A. Bell palsy II Pathogenetic mechanism of idiopathic peripheral facial paralysis. Trans Amer Acad Ophthalm Otolaryng 70 (1966) 381
- BRUNNER S. and PEDERSEN C. B. Roentgen examination of the facial canal. Acta radiol. Diagnosis 10 (1970) 545
- PEDERSEN C. and STOKSTED P. Tomography of the facial canal in non rheumatic facial palsy. Acta radiol. Diagnosis 1 (1963) 90
- ECKERDAL O. Tomography of the temporomandibular joint. Correlation between tomographic image and histologic sections in a three-dimensional system. Acta radiol. (1973) Suppl. No. 329
- FOWLER E. P. Verlaufsanomalien des V. facialis im Schläfenbein. Z. Laryng Rhinol 40 (1961) 360
- GIANGARLO H. R. and MITTUCH H. F. Facial palsy. Facial nerve decompression. Arch Otolaryng 91 (1970) 30
- HARRISON J. A. B. and BURTON E. H. Tomography of the facial canal. An experimental study. J. roy. na. med. Serv. 55 (1969) 166
- JEROME O. Topognosis (topographic diagnosis) of facial nerve lesions. Arch. Otolaryng 81 (1963) 446
- JOWAKES L. B. Bell palsy. A surgical emergency. Arch Otolaryng 81 (1965) 497
- KURTZEL K. Peripheral facial palsy. Pathology and surgery. Munksgaard Copenhagen 1959
- Surgery of the facial nerve. Arch Otolaryng 77 (1963) 327
- MA M. Facial paralysis peripheral type. A proposed method of reporting (Emphasis on diagnosis and prognosis as well as electrical and chorda tympani nerve testing). Laryngoscope 80 (1970) 331
- MILLER H. Facial paralysis. Brit. med. J. 3 (1967) 815
- MISSELER A. Anatomy and clinical aspects of the facial nerve. Arch Otolaryng 81 (1965) 444
- POWELL JR. Bell palsy in pregnancy. Arch Otolaryng 89 (1969) 830
- REICHMANN S. () Development of spurious contours of spherical and cylindrical objects in tomography. Acta radiol. Diagnosis 12 (1972) 317
- (b) Tomography of the lumbar intervertebral joints. Acta radiol. Diagnosis 12 (1972) 641
- ROSWORTH J. R. and POWELL J. W. Bell palsy. A predisposition of pregnant women. Arch Otolaryng 95 (1972) 125
- SALT J. LEVY E. and CHACO J. Surgery and pathology of Bell palsy. Arch Otolaryng 82 (1965) 594
- SATO H. RAY R. R. F. and SCHWENKERT H. F. Course of the sensory component of the nervus intermedius in the temporal bone. Ann. Otol. 79 (1970) 960
- ZILBERMAN PEDERSEN K. Quantitative measurements of the nasolacrimal reflex. In normal and in peripheral facial paralysis. Arch Otolaryng 81 (1965) 457

ANGIOGRAPHIC DIAGNOSIS OF RENAL VEIN THROMBOSIS IN MALIGNANT RENAL TUMOURS

L. HENRIKSSON and C G MIKAELSSON

A decision upon nephrectomy for renal carcinoma is considerably aided by information regarding the state of the renal vein. This vein is often difficult to demonstrate by nephroangiography and may not be filled even by the usual selective technique, i.e. with 8 to 12 ml of a 60 % contrast medium. FOLIN (1967) reported 59 cases in 32 of which neither the renal vein nor any colaterals were visible. Obstruction of the renal vein was observed in 15 cases only; no anatomic explanation was offered in the remaining 17 cases although a large amount of contrast medium was sometimes used, viz 25 ml Urografin 60 %. Other authors, e.g. BJØRSEN & FOLIN (1961) and AHLBERG *et coll* (1966) have arrived at similar results. The phlebographic methods available at present have certain drawbacks: thus only changes reaching the vena cava can be diagnosed by means of cavography. Moreover selective retrograde phlebography may produce the danger of existing thrombi being displaced mechanically. If the contrast dosage be sufficiently raised when performing selective nephroangiography the renal veins will be regularly and sufficiently filled to be scrutinized in detail. An amount of 50 ml Urografin 76 % was injected into the renal artery and a series of films at every other second for about 20 seconds.

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Fig 1 Renal vein with malignant thrombus (selective high dose nephroangiography)

obtained immediately after the ordinary nephroangiography. Such high dosage is permissible only in cases in which conventional angiography has revealed the presence of renal carcinoma and it is obvious that the diseased kidney will have to be removed. Again this technique should be practised only if the neoplasm receives its main blood supply from a single artery. The present material consists of 16 cases of renal carcinoma, all of which were unilateral, 10 right sided and 6 left sided.

Results

Selective high dosage angiography demonstrated well filled veins and collaterals so that it was nearly always possible to examine the renal vein in detail for partial occlusion. A distinct renal vein without any abnormality was evident in 6 of the 10 right kidney and in 3 of the 6 left kidneys. The operation



Fig. 2 Hypovascular renal carcinoma in and around the right kidney with a clusion of the renal vein a) Arterial phase b) Venous phase

specimen never contained a malignant thrombus (Fig. 1). In the 4 other right-sided kidneys high dosage angiography failed to reveal the renal vein, and a thrombus was always present in the operation specimens (Fig. 2). In one of the left-sided cases a definite thrombus appeared as early as the arterial and the nephrographic phases (Fig. 3) but it was also evident that the renal vein itself had been filled with medium in the venous phase: this meant that the occlusion was partial. By comparison, with ordinary dosage the presence of thromboses could be eliminated with certainty in one right-sided case and one left-sided case only. The other cases in which it was possible to discern the renal vein (3 on the right and 1 on the left side) presented an unsatisfactory concentration of medium. Veins free of thrombi failed to appear at all with ordinary doses in 6 cases: for instance the larger of two right renal veins in one case draining the area adjacent to the tumour. The concentration of medium in the collaterals increased with high dosage in 9 cases, and additional veins could be discerned



Fig 3a

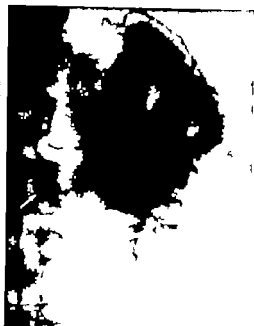


Fig 3b



Fig 4

Fig 3 Hypervascular renal carcinoma of the left kidney with malignant thrombus in the renal vein and partial occlusion. a) Arterial phase with pathologic vessels in venous thrombus (→) b) nephroangiogram in venous phase with partial contrast filling of the vein (→)

Fig 4 Small carcinoma in upper lateral part of the right kidney. The kidney is drained by two veins without thromboses (→) The conventional dosage of medium only revealed the caudal vein

Discussion

The dose of contrast medium in the cases reported is not high from a general point of view. Injury to the kidney may be disregarded as the organ is to be removed. Nor is there any risk of accidental injection into lumbar vessels with the type of catheter employed (MIKELLSSON 1965). With but limited experience of high dosage angiography the present authors allowed some margin when deciding the amount of medium in order to ensure reliable diagnosis of the veins. For the same reason the individual blood flow through the tumours was ignored.

Anatomic examinations by ANSON & CAULDWELL (1947) and others have indicated that more than one vein drains the right kidney in about one fifth of cases. In such cases one vein usually runs from the upper part and one from the lower part of the kidney. About 99 per cent of the left veins occur singly at the hilum of the kidney and their outlet into the vena cava, although they may sometimes bifurcate around the aorta to form a so called peri-aortic ring. A short left renal vein may also open into a persistent left vena cava (1 per cent).

As the right renal vein is sometimes duplicated, venous thrombosis is difficult to make with the same degree of certainty as with the left renal vein. If it is possible to discern two veins draining the right kidney (Fig. 4) or if the tumour is located cranial to a renal vein normally situated, the conclusion may safely be reached that the formation of a thrombus in the lower part of the kidney would be unlikely.

It is somewhat more difficult to make a detailed assessment of the right renal vein than of the left one in cases of partial occlusion. The right vein lies in front of and very close to the kidney; thus latter is filled with medium and rotation of the patient to the left would be required to allow its projection free of adjacent structures, although its medial part and the vena cava might well be obscured by the spine. The medial part of the left renal vein is often also difficult to identify even with high dosage angiography, one reason being that it is concealed by the skeleton (BOJSEN & JOHN 1961). The vein is sometimes to a great extent drained through the left gonadal vein, and thus absence of filling does not necessarily mean that the renal vein is obstructed (ANILBERG *et al.* 1965). It is a known fact that dilated sinuous veins occur around a carcinomatous kidney (LJUNGBERG 1930 and others); with high dosage angiography these were more completely filled than with ordinary selective nephroangiography, and the former was sometimes the only means of detection. The vessels run in various directions in the retroperitoneal space, often for some distance caudally. ANILBERG *et al.* (1966) were of the opinion that the filling of a well developed collateral system around the tumour indicated probable venous blockage. Thrombi in the renal vein in the present small series were not specifically associated with the occur-

rence of collaterals. The development of the latter may depend just as much on the type of tumour, its vascularity and its position in the kidney as on venous blockage (Fig. 2). In the outer layers of the kidney even small tumours sometimes have well developed collaterals even when the renal vein is free.

Selective high dosage angiography in renal carcinoma is a simple method of facilitating examination of the renal venous system and supplying considerably increased information. The absence of filling of a renal vein seems to indicate that it is thrombosed. High dosage angiography often supplies sufficient information and the patient may be spared the strain of cavography which otherwise must be performed in order to locate the part of the tumour that may be growing into the vena cava.

SUMMARY

Selective high dosage nephroangiography was performed in 16 cases of renal carcinoma. In 5 of these with positive findings of malignant thrombosis in the renal vein the condition was evident prior to operation; in all the other cases it could be stated with certainty that no thrombi were present. The method is simple and without harm to the patient and cavography may be avoided. Here the absence of renal vein thrombosis is proved.

ZUSAMMENFASSUNG

Eine selektiv hochdosierte Nephroangiographie wurde bei 16 Fällen mit einem Nierenkarzinom vorgenommen. Bei 5 dieser Fälle mit dem nachgewiesenen Befund einer malignen Thrombose der Nierenvene war diese Veränderung vor der Operation bekannt; in allen anderen Fällen konnte mit Sicherheit festgestellt werden, dass keine Thromben vorhanden waren. Die Methode ist einfach, ohne Schaden für den Patienten, und die Cavographie kann unterlassen werden, da das Fehlen einer Nierenvenenthrombose nachgewiesen ist.

RÉSUMÉ

Les auteurs ont fait une angiographie rénale sélective à forte dose dans 16 cas de cancer du rein. Dans cinq de ces cas les signes de thrombose maligne de la veine rénale ont été évidents et le diagnostic était évident avant l'opération. Dans tous les autres cas on pouvait affirmer avec certitude qu'il n'y avait pas de thrombose. Cette méthode est simple et sans inconvénient pour le malade. Elle permet d'éviter la cavographie quand il est prouvé qu'il y a pas de thrombose de la veine rénale.

REFERENCES

- ANDERSON, V. E., BARTLEY, O. and CHURCH, L. N. Retrograde contrast filling of the left gonadal vein. A roentgenologic and anatomical study. *Acta radiol. Diagnosis* 3 (1965) 385.
- and WAHLQVIST, L. Angiographic diagnosis of tumor thrombus in the main trunk of the renal vein in renal carcinoma. *Acta chir. scand.* 132 (1966) 362.

- ANSON B. J. and CAULDWELL E. W. The perirenal vascular system. A study of 475 anatomical specimens. *Quart. Bull. Northwest Univ. med. Sch.* 21 (1947) 320.
- PICK J. W. and BEATON L. E. The blood supply of the kidney, suprarenal gland and associated structures. *Surg. Gynec. Obstet.* 84 (1947) 313.
- BOJEN E. and FOLIN J. Angiography in the diagnosis of renal carcinoma. *Radiologe* 1 (1961) 173.
- FOLIN J. Angiography in renal tumours. *Acta radiol.* (1967) Suppl. No. 267.
- Lt. GREN C. Studien über Klinik und Prognose der Grauerischen Nierentumoren zugleich ein Beitrag zur Frage nach der Genese der Hamatur. *Acta chir. scand.* (1930) Suppl. No. 16.
- MIKAELSSON C. O. Polythene catheter of new shape for percutaneous selective catheterization. *Acta radiol. Diagnosis* 3 (1965) 581.

HIGH DOSE UROGRAPHY IN ADVANCED RENAL FAILURE

I Evaluation of diagnostic value

P STAGE N MILMAN and EVELYN BRIK

Following the introduction of the less toxic triiodinated contrast media for urography in 1953 (the diatrizoates) more than 10 years elapsed before the higher doses were employed in renal failure (SCHWARTZ et coll 1963 SCHENCKER 1964). This reluctance was due to experiences with the earlier diiodinated contrast media which frequently caused deterioration of renal function even in low doses and furthermore produced poor diagnostic results (OLSSON 1954).

High dose urography has been applied to patients with marked renal failure even in a state of anuria in recent years (FRY & CATTILL 1971 BROWN et coll 1970). The diagnostic results were encouraging and the examinations were apparently not followed by further depression of renal function; its systematic recording before and after urography was however not performed.

The value of high dose urography in advanced renal failure is however not generally accepted and the present investigation was therefore undertaken first to assess the diagnostic information in extremely uremic patients all having endogenous creatinine clearances less than 12 ml per minute with several already in dialysis and secondly to determine the effect of the contrast medium on renal and hepatic functions. A number of patients were examined both before

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- ANSON B. J. and CAULDWELL E. W. The perirenal vascular system. A study of 425 anatomical specimens. *Quart Bull Northwest Univ. med Sch* 21 (1947) 320
- PICK J. W. and BEATON L. E. The blood supply of the kidney, suprarenal gland and associated structures. *Surg Gynec Obstet* 84 (1947) 313
- BOTJEN E. and FOLIN J. Angiography in the diagnosis of renal carcinoma. *Radiologe* 1 (1961) 173
- FOLIN J. Angiography in renal tumours. *Acta radiol* (1967) Suppl. No. 267
- LYNGGREN C. Studien über Klinik und Prognose der Grawitzschen Nierentumoren zugleich ein Beitrag zur Frage nach der Genese der Hamaturie. *Acta chir scand* (1930) Suppl. N. 16
- MIKAELSSON C. G. Polythene catheter of new shape for percutaneous selective catheterization. *Acta radiol. Diagnosis* 3 (1965) 581

Table 2

The distribution of the 50 patients according to the main diagnosis

Diagnosis	No. of cases
Chronic pyelonephritis	15
Acute episode in chronic pyelonephritis	2
Chronic glomerulonephritis	10
Subacute glomerulonephritis	3
Nephrosclerosis	7
Polycyst kidneys	5
Acute tubulointerstitial nephropathy	4
Histiocytic nephropathy (Alport)	1
Medullary cyst kidneys	1
Chronic nephropathy unknown type	2
Total solitary kidneys in this group	
Histologic confirmation of diagnosis in 3 patients	

creatinine and creatinine clearance indicated that renal function was stationary in the week prior to urography (steady state uremia). Group 3 consisted of patients with acute exacerbation in chronic renal failure. One had a single dialysis before urography. Group 4 finally contained patients in acute renal failure. One had a single dialysis before urography and another was examined both before and after dialysis. The diagnoses of the underlying diseases appear in Table 2.

Technique of urography. Specific instructions were given to a oral fluid restriction and laxatives. Premedication consisting of chlorpromazine 25 mg i.m. and antazoline 50 mg i.m. was given one hour before urography.

Initial ordinary tomography (linear tomograph multicassette 60 to 70 kV, 130 mA, 4 s) was performed to evaluate the data for correct exposure and cuts and to identify renal outlines and calculi. The contrast medium 150 ml sodium and methylglucamine diatrizoate (Urografin 76[®]) was given undiluted as a single intravenous injection during 2 to 5 minutes. One patient (weight 30 kg) received only 100 ml. The dose amounted to 1.5 to 3.7 ml per kg body weight, mean 2.5 ml/kg. No urticaria or compression was applied. Tomograms were obtained immediately after the injection and usually 10 to 20 minutes later. If the renal delineation was satisfactory and the pelvicalyceal system demonstrated no later films were taken; if not further tomography was performed.

The films were evaluated independently by two of the authors. Special attention was paid to renal size and delineation, the presence of a nephrogram, the delineation of the pelvicalyceal system and any sign of obstruction.

Table 3

Size of unobstructed kidneys in chronic and acute renal failure. Long axis of kidneys (including about 12 per cent magnification)

Diagnosis	N of kidney	Range (cm)	Mean (cm)
Polycystic kidney	10	20.0-23.0	20.6
Chronic pyelonephritis	28	7.5-12.5	10.1
Chronic glomerulonephritis	20	8.5-13.0	10.1
Acute tubulointerstitial nephropathy	8	14.0-16.5	15.2

The delineation of each calyx system, the pelves and ureters were assessed and categorized as good (2 points) satisfactory (1 point) or non demonstrable (0 point) (In two single kidney patients the sum of points was doubled) Thus the total sum of points in every examination might vary from 0 to 12 points

Results

Renal outline and size Before the contrast injection, 46 of the 98 kidneys were well outlined and 26 were partially delineated. In 26 cases the size of the kidneys could not be determined. After contrast injection, 86 were clearly delineated. Among 12 kidneys that were not well outlined 10 were polycystic. A nephrographic phase was obtained in all but one patient with acute oliguric tubulointerstitial nephropathy and a creatinine clearance of 0.3 ml/min: the kidneys were clearly delineated before the injection.

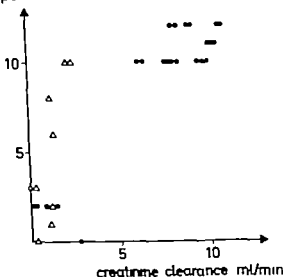
Table 3 presents the size of kidneys in chronic and acute renal failure. A distinct difference between three groups is noted: the very large polycystic kidneys, the moderately enlarged kidneys in acute tubulointerstitial nephropathy and the small kidneys in chronic pyelonephritis and chronic glomerulonephritis.

Table 4

Urography in diagnosis of obstruction

Obstruction	N of cases
Eliminated both sides	44
Present one side, eliminated other side	4
Unknown both sides	2
Total	50

points



Correlation between creatinine clearance and the filling of the collecting system (in points from 0 to 12) ○ diuresis < 100 ml/4 h Δ diuresis 100 to > 300 ml/4 h ● diuresis > 300 ml/24 h

Four patients with chronic pyelonephritis and unilateral obstruction (all right sided) had the long axis of the obstructed kidneys exceeding the contralateral by 1 to 2 cm

The collecting system and obstruction Some parts of the collecting system were demonstrated in 93 kidneys. Urinary obstruction could be excluded bilaterally in 44 patients (Table 4). In one kidney without filling of the pelvicalyceal system obstruction could be eliminated by the presence of non-dilated calyces contrasting the nephrogram. Unilateral obstruction was diagnosed in 4 patients from dilation of the upper urinary tract (necrotic papilla obstructing the ureter, 3 stone obstructing the ureter, 1 patient). The presence or absence of obstruction was undeterminable in 2 patients. In the first a patient in chronic dialysis (creatinine clearance 2.7 ml/min) the nephrogram revealed very large kidneys with multiple filling defects enabling the diagnosis of polycystic kidneys although no filling of the pelvis could be obtained. Urinary obstruction was excluded by retrograde pyelography. The second patient suffered from acute oliguric tubulo-interstitial nephropathy (creatinine clearance 0.3 ml/min). The kidneys were moderately enlarged but no nephrograms or filling of the pelvicalyceal system could be produced. Repeat urography in the following polyuric stage (creatinine clearance 7.8 ml/min) indicated decreasing renal size, distinct nephrograms and non-obstructed pelvis and calyces.

Table 5

Effect of dialysis on the concentration of glomerular filtrate, serum osmolality and the filling of the collecting system at intravenous urography

Case No.	Creatinine clearance ml/min	Serum creatinine mmol/l	Serum urea mmol/l	U/P ratio for creatinine	Serum osmolality mmol/l	Increase of filling
		Before—after	Before—after	Before—after	B before—after	After
1	4.7	1.23—0.93	40—23	2.9—5.7	304—28	no
2	2.2	1.73—0.93	18—10	6.0—12.6	313—302	no
3	2.7	1.33—0.59	31—9	3.2—7.8	318—282	no
11	1.2	1.64—1.23	40—18	3.1—5.7	347—330	no
24	1.2	1.24—0.93	42—6	3.8—7.2	320—289	yes
29	10.2	0.83—0.50	47—22	5.4—10.2	310—	no
33	5.0	1.17—0.56	67—19	4.2—9.5	345—316	yes
Mean	3.9	1.31—0.81	41—15	4.1—8.4	322—300	

The figure presents the correlation between creatinine clearance, diuresis and filling of the collecting system according to the previously mentioned system of graduating the outlining and filling of the pelvicalyceal system in each urography. It appears that rising creatinine clearance increases the filling of the pelvicalyceal system although a considerable deviation is evident. With decreasing body weight and consequently increasing contrast dose per kg body weight, the average quality was improved. No correlation was obtained between the filling of the collecting system and U/P ratio for creatinine.

Urography was performed in 7 patients in chronic dialysis before and immediately following dialysis. Table 5 presents the renal function (creatinine clearance) and the effect of dialysis upon the concentration of glomerular filtrate (U/P ratio for creatinine), serum creatinine, serum urea, serum osmolality and the filling of the pelvis. A comparison between pre-dialytic and post-dialytic uroographies indicated in 2 patients improved filling after dialysis while in 5 patients no significant difference was present. Before dialysis parts of each collecting system were apparent and obstruction excluded in all but one patient (Case 3 polycystic kidney). Dialysis failed to improve the quality in this patient. The advantage of pre-urographic dialysis therefore seems to be negligible.

Serum osmolality before and 10 minutes after the injection of 150 ml Urografin 76% was recorded in 11 uroographies (Table 6). A considerable increase in serum osmolality (average 4.5 per cent) was noted in all patients.

The high dose of contrast medium was well tolerated even by patients in poor general condition and with pulmonary congestion. Anti-emetic and anti-

Table 6

Serum osmolality before and 10 minutes after injection of 150 ml Urografin 76

	Serum osmolality (mOsmol/l)		
	Before	After	Increase
	304	311	7
	285	310	25
	313	321	8
	309	314	19
	318	332	14
	287	29	13
	338	47	9
	297	315	18
	312	322	10
	347	358	11
	309	332	23
Mean	310	323	14

allergic premedication was administered in 50 urographies in which no nausea vomiting or immediate allergic reactions were observed. One patient developed exanthema after the examination. Fifteen patients complained of a sensation of heat during the injection. No premedication was given in eight cases among these 8 patients 3 had nausea and vomiting, 1 urticaria and 1 a sensation of heat. The frequency of thirst and of a sensation of heat increased with the dose of contrast medium per kg body weight.

Discussion

For the management of patients admitted with severe renal failure the primary role of urography is to evaluate the size of the kidneys (and thereby the stage of the disease) and to exclude extrarenal obstruction. Furthermore information about renal outline and the number and position of the kidneys is of importance in the indication for renal biopsy. Satisfactory urography may often save the patient from more arduous examinations such as retrograde pyelography, nephroangiography and renal biopsy.

High doses of contrast media must be administered to compensate for decreased renal function and tomography must also be employed to outline the upper urinary tract. Fluid restriction and laxatives are generally avoided in order to reduce the risk of further renal impairment (FRY & CATTELL BROWN *et coll.*).

DACIE & FRY (1971) demonstrated in patients with normal renal function that the sodium salt of diatrizoate gave better filling of the pelvicalyceal system than the methylglucamine salt while McCLENNAN & BECKER (1971) were unable to confirm these results and considered the difference between the two salts to be of no clinical importance. Earlier experiences of the present authors with urography in renal failure (STAGE *et coll.* 1971) indicated the value of Urografin 76 % a mixture of the two salts. The dose employed was high, with an iodine content varying from 0.56 to 1.37 g iodine per kg body weight (mean 0.93 g/kg). In recently published series (MAHAFFY *et coll.* 1969 FRY & CATTELL BROWN *et coll.* MATALON & EISINGER) maximal doses of sodium diatrizoate of 0.59 to 0.64 g iodine per kg body weight were applied.

MAHAFFY *et coll.* in 33 patients with acute or acute in chronic renal failure examined after dialysis, delineated renal outline in 91 per cent, obtained a nephrogram in 54 per cent, and demonstrated parts of the collecting system in 85 per cent of the kidneys; they thus excluded or confirmed obstruction in 85 per cent of the kidneys.

FRY & CATTELL defined renal outline in 92 per cent, obtained nephrograms in 81 per cent and demonstrated parts of the collecting system in 91 per cent of the kidneys in 48 non oliguric patients with creatinine clearance below 10 ml/min. They were thus able to demonstrate or exclude renal obstruction in 91 per cent of the kidneys.

BROWN *et coll.* demonstrated renal delineation in 95 per cent, obtained a nephrogram in 95 per cent and demonstrated parts of the collecting system in 54 per cent of kidneys in 22 oliguric or anuric patients, 12 of whom were treated with dialysis. Thus, obstruction was confirmed or ruled out in 54 per cent. In the remaining 46 per cent of the kidneys the size of the calyces contrasting the nephrogram was used in assessing the question of obstruction. The authors stated that it seems likely that extra renal obstruction can be excluded even when the pelvicalyceal system is not filled, provided there is a definite nephrogram and the contrasting calyces are not dilated. Obstruction was excluded in this way in the present series in only one kidney. On the other hand it would appear that the presence of apparently dilated calyces does not necessarily indicate obstruction. Especially in patients with chronic pyelonephritis the fat tissue in the renal sinus is often significantly increased and if no filling of the pelvicalyceal system is evident this may simulate dilated calyces (OLSSON & WERLAND 1963).

The present authors were able to determine the renal size in 100 per cent and the total renal delineation in 86 per cent of the kidneys. Distinct nephrograms were obtained in 98 per cent and parts of the collecting system in 93 per cent of the kidneys; obstruction was demonstrated or ruled out in 96 per cent.

MATALON & EISINGER performed urography before and after dialysis with 2.2 ml Hypaque 50 % (sodium diatrizoate) per kg body weight in a drip infusion equivalent to 0.64 g iodine per kg in 8 patients in chronic dialysis (creatinine clearance 0.4 to 10.0 mean 5.2 ml/min). In the pre-dialytic urographs no parts of the collecting system were ever defined while in the post-dialytic examinations this occurred in 6 patients all had a post dialytic U/P ratio for creatinine above 16 with the exception of 2 patients with ratios about 9. The authors concluded that filling of the pelvicalyceal system is possible only if this ratio is higher than about 12 and in order to increase the ratio in azotemic patients they recommended intensive dialysis prior to urography. The present material comprised 7 patients (Table 5) in chronic dialysis with creatinine clearances between 1.2 and 10.2 ml/min (mean 3.9 ml/min) and in a slightly more uremic state as judged from the serum urea level than the patients of MATALON & EISINGER. The average U/P ratio for creatinine was 4.1 before and 8.4 after dialysis. The quality of dialysis estimated from the decrease in serum urea was comparable to the series of MATALON & EISINGER. The present authors obtained filling of the collecting system both before and after dialysis in all but one patient (Case 3). Only in two cases (Nos 24 and 30) did the filling improve after dialysis. These 2 patients had the most marked decrease in the serum urea after dialysis, but not the greatest increase in U/P ratio for creatinine.

The results of MATALON & EISINGER thus appear to remain unconfirmed. An explanation for our better results may be the employment of a higher contrast dose apparently reducing the demand for pre urographic dialysis. The present authors have employed as a routine the highest doses so far reported. SPERWOOD *et coll* (1968) administered Urografin 60 % 4 ml per kg body weight (1.2 g iodine/kg) in 5 patients but observed constant side effects described as a period of malaise and shivering. Twelve patients of the present material received a dose with an iodine content higher than 1.2 g/kg all without these serious reactions. It would appear that anti-emetic premedication has not been used in other series. The effect upon nausea and vomiting was obvious while the sensations of heat and thirst were unaffected. The sensation of thirst is well explained by the demonstration of a considerable increase in serum osmolality following the injection of contrast medium.

In conclusion high-dose urography with tomography has proved to be a valuable diagnostic tool in the evaluation of severe renal insufficiency even in anuric and oliguric patients. The diagnostic results have generally speaking been in accordance with the above mentioned recently published series. Any slightly better results may be explained by the employment of a higher dose of contrast medium.

SUMMARY

High dose urography including tomography with 150 ml Urografin 76 % and anti emetic premedication was performed in 50 patients with advanced renal failure with creatine clearance below 12 ml/min. 7 were examined both before and after dialysis. Renal ure reflecting the duration of the disease could be determined in 100 per cent. Nephrograms and filling of the collecting system of the kidneys to exclude or confirm obstruction were obtained in about 96 per cent. Pre urographic dialysis did not improve the diagnostic quality.

ZUSAMMENFASSUNG

Hochdosierte Urographie einschließlich Tomographie mit 150 ml 76 % igem Urografin und antiemetischer Vorbehandlung wurde bei 50 Patienten mit fortgeschrittenen Nierenschäden mit einem Kreatininclearance unter 12 ml/min. vorgenommen. 7 Patienten wurden vor und nach einer Dialyse untersucht. Die Nierengramme ein Mass für die Dauer der Erkrankung konnte in 100 % bestimmt werden. Nephrogramme und Pyelogramme der Nieren um eine Obstruktion auszuschliessen oder zu sichern wurden etwa 96 % erhalten. Eine Dialyse vor einer Urographie verbesserte nicht die diagnost. Qualität.

RÉSUMÉ

Les auteurs ont fait des urographes à forte dose et des urotomographes avec 150 ml litres d'ografine à 76 % et une prémédication antiémétique chez 50 malades atteints d'insuffisance rénale à créatinine inférieure à 12 millilitres par minute. Sept de ces malades ont été examinés avant et après dialyse. L'indication des reins exprimant la durée de la maladie a pu être déterminée chez tous les malades. Les auteurs ont obtenu des néphrographes et des pyélographes des reins afin d'exclure ou d'affirmer l'obstruction dans environ 96 % des cas. Une dialyse avant l'urographie n'a pas amélioré la qualité diagnostique.

REFERENCES

- BROWN C. B., GLAWAY J. J., IRY I. K. and CATTALL W. R. High dose excretion urography in oliguric renal failure. *Lancet* 1970 II p. 932.
- DACEY J. T. and IRY I. K. A comparison of sodium and methylglucamine diatrizoate in clinical urography. *Brit. J. Radiol.* 44 (1971) 1.
- IRY I. K. and CATTALL W. R. Excretion urography in advanced renal failure. *Brit. J. Radiol.* 44 (1971) 198.
- MARTIN R. G., MITCHELL N. A. and CARROLL D. T. Infusion pyelography in acute renal failure. *Clin. Radiol.* 20 (1969) 320.
- MATALON R. and EMMERT R. P. Successful intravenous pyelography in advanced uremia—urinalization in the post-dialytic state. *New Engl. J. Med.* 282 (1970) 835.
- MCCLENNAN B. I. and BRIDGES J. A. Excretory rography: choice of contrast material—*Clinical Radiology* 100 (1971) 591.
- OLSON O. Contrast media in diagnosis and attendant risks. *Acta radiol.* (1971) Suppl. V 116.
- and WETLAND I. O. Renal fibromatosis. *Acta radiol. Diagnosis* 1 (1963) 1061.

- SCHENCKER B. Drop infusion pyelography: indications and applications in urologic roentgen diagnosis. *Radiology* 83 (1964) 12.
- SCHWARTZ W. B., H. RYFT A. and EITTINGER A. Intravenous urography in the patient with renal insufficiency. *New Engl J Med* 269 (1963) 277.
- WILKINSON T., BRIDGEMAN A., DOLLEY C. T. et coll. Intravenous urography and renal function. *Clin Radiol* 19 (1968) 296.
- YAGI P., BALK E., FOLKE K. and KARL A. Urography in renal failure. *Acta radiol. Diagn* 11 (1971) 337.

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SLOW INJECTION HEPATIC ANGIOGRAPHY

A comparison with a high injection rate

J. KAUDE, R. JENSEN and G. W. WERTANEN

Malignant lesions of the liver whether primary or metastatic may be treated by partial hepatectomy or by continuous intraarterial infusion of cytotoxic agents. These methods of treatment although usually palliative require knowledge of the vascular anatomy of the liver and of the site of the tumour within the liver information that may be obtained by hepatic angiography. Although angiography for detection of hepatic tumours has been used for more than 20 years (BIERMAN *et coll* 1951) and numerous reports have been published (BOIJSEN & ABRAMS 1965, BARTLEY *et coll* 1969, KAUDE & RIAN 1971, WATSON & BALTAXE 1971 and others) the results for small hypovascularized tumours still remain unsatisfactory. The size limit for demonstration of metastatic lesions in the liver with selective hepatic angiography is approximately 0.5 to 1 cm for highly vascularized

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Table

Slow injection hepatic angiography in 52 patients (53 examinations)

Site of primary tumour with hepatic metastases verified angiographically and histologically		Other lesions		Normal findings or probable regeneration nodules
Pancreas	2	Cirrhotic	3	
Oesophagus	2	Haemangioma	1	
Colon or rectum	7	Abscess	1	
Kidney	2	Trauma	1	
Liver	3	Haematoma		4
Common bile duct	1	secondary to		
Unknown (poorly differentiated adenocarcinoma or further investigation not performed)	5	biopsy	3	
	27		9	

patients with liver cirrhosis and superimposed hepatocellular carcinoma included in both columns

Examined twice with repeat angiograph normal

4 patients with known primary malignancy (carcinoma of colon, rectum or pancreas and one melanoma). Hepatic biopsy or exploration for metastases or cirrhosis negative.

and 2 to 5 cm for poorly vascularized tumours (BOIJSEN 1965; BARTLEY *et coll* 1969) the size limit stresses the necessity to improve the angiographic techniques.

Hepatic angiography performed with a large quantity of contrast medium (50 to 75 ml) injected selectively into the hepatic artery over 10 to 40 s has been performed for catheter and tumour localization and in the follow up of tumours treated with intraarterial infusion therapy (WIRTANEN *et coll* 1968—1971) KAUDE & WIRTANEN 1970; WILLIAMS & WISE 1970). The long injection time through indwelling catheters without sideholes was necessary because of the length or small diameter of the catheter. Good results with this technique have however been reported (WIRTANEN 1970, 1971). These findings initiated comparison with angiography performed at an injection rate of 10 to 12 ml/s. A preliminary report of this work has recently been presented (JENSEN & KAUDE 1971).

Material and Methods Fifty two patients were examined by hepatic angiography with both high and low injection rates at the same session. For the examination at the high injection rate 30 to 50 ml Iopaque 76% depending on the size of the catheterized vessel were injected through a polythene catheter



b

Fig. 1. Hepatic metastases of poorly differentiated adenocarcinoma. Sel. arteriogram: a) 40 ml contrast medium 76% injected at 9 ml/s; b) 50 ml contrast medium 11/5 ml/s. Right upper part of right liver lobe and better defined nodules. The periphery of necrotic nodules with low injection contrast rate.

(ID 1.45 mm, OD 2.2 mm) at a pressure of 2.5–3 kg/cm². If injection time was recorded with a Mingograf and varied between 3 and 4.5 s at a rate usually of 10 to 12 ml/s. Serial stereoscopic radiography was performed with an overhead tube (focal spot 1 mm) and a 35 cm × 35 cm cut film changing one film/s for 2 s, 2 films/s for 4 s and one film every other second for 12 s. Overexposure, a total time of 18 s.

Angiography at a slow injection rate was effected with 50 ml contrast medium (30 or 40 ml in a few patients) carried out at a pressure of 1 to 1.5 kg/cm² resulting in injection times between 8.5 and 14 s but usually 10 to 12 s and injection rates of about 2.5 to 5 ml/s. Films were usually exposed at 2 s intervals for 32 s. The catheter in all the slow injection examinations was placed in the common right or left hepatic artery. With the rapid injection the tip of the catheter lay in one of the hepatic arteries at 33 examinations (one patient was examined twice) and in 20 patients in the coeliac axis or depending on the origin of the hepatic artery in the superior mesenteric artery.



Fig. Primary hepatocellular carcinoma. Selective angiography of an intermediate branch of the hepatic artery: a) 40 ml contrast medium at 10 ml/s; b) 30 ml at 5 ml/s. The accumulation is better in the malignant nodules even when less contrast medium is used.

Results

The angiographic findings, the site of the primary tumour and the presence of hepatic metastases appear in the Table. Malignant nodules were demonstrated better or solely by slow injection in 14 of 22 patients with verified metastatic lesions of the liver (Figs 1-3). The slow and rapid injection techniques were diagnostically of equal quality in 8 patients. The rapid technique never afforded information in any patient with a hepatic tumour better than that produced by the slow injection method.

The small malignant nodules were always well circumscribed and hypervascular (Figs 1 to 4). Larger nodules frequently had a large poorly vascularized area centrally and the well vascularized periphery tended to become smaller (Figs 1, 4, 5); its width in some nodules was only 2 mm (Fig. 5). The origin of the primary tumour could not be determined from the angiographic appearances of the metastases.

The patient who was examined following blunt abdominal trauma proved to have intrahepatic haematomas, extravasation of contrast medium and arteriovenous shunting secondary to traumatic injury to the liver parenchyma (Bojarski et al. 1971) and the lesions were demonstrated only by slow injection (Fig. 6).

One of 3 haematomas secondary to liver biopsy was demonstrated better by slow injection as was the liver abscess in one patient and the haemangioma in another patient. Small hypervascularized but irregular nodules quite unlike

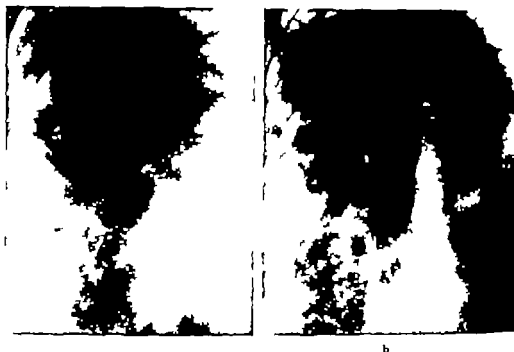


Fig. 3. Hepatic metastases of unknown origin. Selective angiography of right hepatic artery. Comparison of a) rapid injection rate (50 ml at 7 ml/s) and b) slow injection (50 ml at 4 ml/s). Better demonstration of neoplasms with higher concentration of contrast medium in the nodules and less contrast in the normal liver tissue with slow injection.

metastatic lesions in appearance, were revealed by slow injection in 12 patients (Figs 7-8). Three of these had hepatic carcinomas verified either by biopsy or by the angiographic demonstration of a venous collateral flow secondary to portal hypertension. Four patients with irregular hypervascularized hepatic nodules had a known malignant growth elsewhere but biopsy was negative for metastases or the liver was normal at laparotomy (Figs 7-8). This type of nodularity could not be demonstrated by angiography performed at the rapid injection rate.

Hepatic veins were filled in a total of 27 examinations (51 per cent) by the slow method (Fig. 9). The frequency of vein demonstration was higher in examinations with normal findings (15/21, 71 per cent) than in those with growths (12/22, 52 per cent). The veins were demonstrated in approximately 40 per cent of the selectively injected cases with the rapid injection and in only one by injection into the coeliac axis.



Fig 4



Fig 5

Fig 4 Metastases from cholangiocarcinoma of common bile duct Transbrachial catheterization of left hepatic artery 50 ml contrast medium at 5 ml/sec. Smallest hypervascular growths about 3 mm in size while larger metastases with poorly vascularized centres remain hypervascular at the periphery they are well demonstrated because of the complete wash out of contrast medium from the normal liver tissue by portal flow

Fig 5 Hepatic metastases from carcinoma of the rectum Selective right hepatic angiography with slow injection (40 ml contrast medium at 6 ml/sec) All large hypovascular probably necrotic tumour nodules have narrow richly vascularized rim at the periphery

Discussion

The angiographic diagnosis of well vascularized hepatic tumours depends upon the presence of a neoplastic vasculature possibly terminating in arteriovenous shunting of contrast medium. Poorly vascularized tumours are usually diagnosed by vessel displacement and by filling defects appearing during the capillary phase in the liver with normal tissue homogeneously loaded with contrast medium. Some primary hepatic neoplasms such as cholangiocarcinoma may infiltrate or occlude vessels and hepatomas have the tendency to obstruct the portal vein.

Angiographic examination for the demonstration of malignancy have in the past been performed by delivering as much contrast medium as possible in the shortest possible time to obtain high contrast concentration in the area of interest. Slow injection rates were employed during or following intraarterial infusion therapy with cytotoxic agents to avoid recoil of the infusion catheter

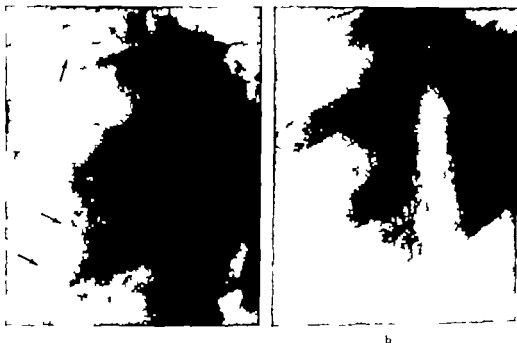


Fig. 6 Hepatic contusion secondary to blunt abdominal trauma. a) Selective slow inject common hepatic angiography. Extravasation of contrast medium shunting to the hepatic vein (→) and inhomogeneous parenchymal take up of contrast medium indicating the presence of several haematomas demonstrated only by slow injection. b) Celiac angiography for comparison.

(WIRTANEN *et coll.* 1968—1971; WILLIAMS & WISE 1970). This low pressure injection is generally thought to degrade the examination because of an inadequate concentration of contrast medium in the tumour. Four probable explanations why metastases in the liver may be better demonstrated by the slow injection rate are suggested.

1) Primary and metastatic tumours in the liver are supplied only arterially (BREEDIS & YOUNG 1954; HEALEY 1965) and as observed angiographically by many authors.)

2) The blood flow through the tortuous, irregular neoplastic vessels that often lack both the muscular layer and elastic lamellae (INDORF 1945) even with some arteriovenous shunting present, is slow.

3) The liver has a double blood supply with approximately 70 to 75 per cent of the flow from the portal vein and 25 to 30 per cent from the hepatic artery (SCIENK *et coll.* 1962). Venous return from the splenic and superior mesenteric veins clears the contrast medium rapidly from the normal liver tissue. Portal vein branches although occasionally obstructed by the tumour do not contribute to



Fig 7 Patient operated upon for pancreatic carcinoma 1966. Pulmonary metastases 1971. Slow injection angiography of the common hepatic artery indicates tortuous hepatic arteries and multiple small hypervascularized nodules throughout the liver probably regeneration nodules. Scintigraphy and needle biopsy revealed no evidence of metastatic lesions or carcinoma.

its blood supply and thus the portal flow will not clear the medium that accumulates in neoplastic vessels during slow injection. The portal vein flow therefore increases the contrast difference between normal and tumour liver tissue (Figs 3-4).

4) The use of relatively large quantities of contrast medium (usually 50 ml for the injection into even small hepatic arteries) results in a high concentration in neoplastic vessels and further enhances the accumulation within the growth (Figs 1-3-4-10) although occasionally the slow injection itself seems to be more important (Fig 2).

Authors have used the term *acalculous tumours* particularly when describing hepatic tumours when no neoplastic vessels could be demonstrated: the diagnosis has rested upon filling defects in the hepatographic phase, vessel displacement or vascular occlusion. It is obvious however that all neoplasms require a vascular supply for their survival and growth. The malignant nodule



Fig. 8

Fig. 8. Carcinoma of the rectum. Small hypervascular, somewhat irregular nodules in right hepatic lobe demonstrated by slow injection angiography. At operation the liver was normal on inspection and palpation.

Fig. 9. Normal hepatic slow injection angiography. Homogeneous capillary phase with filling of the hepatic veins.

is initially hypervascular (Figs 1-4) but as growth proceeds peripherally it is possible that the central area will have become well established and require progressively less arterial blood: the area thus becomes less vascularized to allow diversion of blood flow to the peripheral growth zone. It is also possible that just as the neoplasms produce a steal of blood from normal tissue such a steal may also develop from their central part. The central area then has only enough vascularity to ensure continued survival until cell death and necrosis occur: its usefulness as the site for the establishment of the metastases has been exhausted although a thin hypervascular peripheral zone in the metastatic tumour continues to exist (Fig. 5). This increased number of vessels in the tumour periphery has

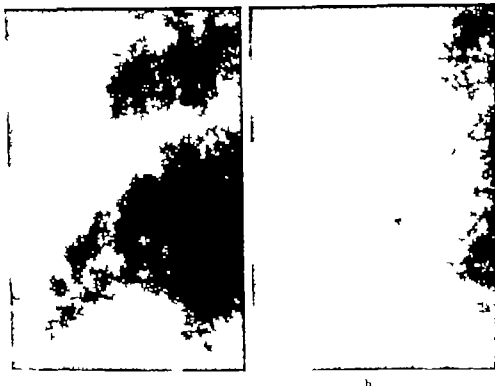


Fig. 10 Hepatic metastases from pancreatic carcinoma. Selective common hepatic angiography. Injection rate the same (5 ml/sec) for both examinations. Better demonstration of the metastases with b) 50 ml contrast medium compared with a) 30 ml.

been discussed by LINDGREN (1945) in a comparison of postmortem arteriograms with the histologic angioarchitecture of neoplasms. He explained the presence of dilated neoplastic vessels in the periphery of necrotic growths by intravital congestion secondary to blood vessel compression caused by the growing tumour. Experimental investigations have indicated that rich peripheral vessels and central necrosis develop when the new growth receives its vascular supply by multiple penetrating arteries from the normal host tissue (RUBIN & CASARETT 1961). The development of central necrosis surrounded by intact malignant cells in an area that remains well vascularized also occurs in active human bronchial carcinomas (THOMLINSON & GRAY 1955).

The same appearances are characteristic of metastatic liver lesions from various primary malignancies. The so-called avascular tumours in the liver with slow injection angiography indeed have a hypervascular periphery, probably not con-

sisting of compressed neoplastic or normal liver vessels but the vital zone of the neoplasm.

Two factors are essential for this improved angiographic technique. First, the catheter must be placed in one of the hepatic arteries and reflux of contrast medium into the coeliac axis or the superior mesenteric artery must be avoided. If reflux occurs, portal flow from the spleen or bowel will contain contrast medium and the contrast difference between the tumour and normal hepatic tissue will be lower; the wash-out of the sinusoids is accomplished by blood mixed with contrast medium. Secondly, contrast medium clearing from the normal liver sinusoids requires good portal vein flow. Slow injection hepatic angiography is not as informative in portal vein obstruction or in severe hypertension with collateral venous flow from the superior mesenteric vein and the splenic vein as in the presence of an intact portal blood flow. It is possible that further improvement to enhance demonstration may occur when pharmacologic agents, such as bradykinin or tolazoline, are injected into the superior mesenteric artery to increase the blood flow from the bowel, while simultaneous slow injection angiography is performed through a second catheter in the hepatic artery.

Enough experience with slow injection angiography to evaluate conditions other than hepatic tumours does not yet exist. The uptake of contrast medium in the liver in verified hepatic cirrhosis was sometimes inhomogeneous and small hypervascularized, usually irregular nodules were demonstrated. Similar regenerating liver nodules occurred in a few patients in whom there was no clinical or histologic evidence of hepatic cirrhosis.

The number of patients with other hepatic lesions such as injury secondary to blunt abdominal trauma or hepatic biopsy and inflammatory disease was too small to determine the value of slow injection. However, in the patient with traumatic injury to the liver, such injection was clearly superior to the conventional method.

Additional information often obtained by slow injection angiography was the frequent demonstration of hepatic veins. Those draining hypervascularized tumours were easily demonstrable (KAUDE & WIRTANEN 1970; WIRTANEN 1971); it is probable that early filling of hepatic veins may indicate the presence of localized inflammatory lesions in the liver (HAWKINS & KAUDE; ALMEN (1966) however was unable to demonstrate hepatic veins by selective hepatic angiography). GLICKMAN & HANDEL (1972) recently reported filling of hepatic veins in only 3 of 50 patients with normal angiographic findings but more often (5 of 6 patients) when the portal flow to a normal liver was reduced. More contrast medium is injected selectively by slow injection into the hepatic artery and the demonstration of hepatic veins is more frequent even when the portal flow is normal.

Multiple hypervascularized tumours tend to retain contrast medium in neoplastic vessels and the amount injected is not always sufficient for the filling of hepatic veins. The relatively large amount of contrast medium is certainly of significance in demonstrating shunting into the portal system, either in malignancy (HAUDE & WERTANEN 1970) or in trauma and is essential for better filling of neoplastic vessels.

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SUMMARY

Hepatic angiography performed with contrast medium injected selectively into the hepatic artery at a rate of 3 to 5 ml/s is an improvement in the technique in the diagnosis of hepatic tumours and seems likely to be useful in demonstrating other hepatic lesions. The essential factors for successful hepatic slow injection angiography are selective hepatic artery catheterization, avoidance of reflux, an intact portal flow, and large amounts of contrast medium.

ZUSAMMENFASSUNG

Die Leberangiographie bei der das Kontrastmittel mit einer Geschwindigkeit von 3 bis 5 ml/s selektiv in die Arteria hepatica injiziert wird, bildet eine Verbesserung der Methode zur Diagnose von Lebertumoren und scheint ebenfalls zum Nachweis anderer Leberläsionen brauchbar zu sein. Die wesentlichen Faktoren für eine erfolgreiche Leberangiographie mit langsamer Kontrastmittelinjektion sind selektive Katheterisierung der Arteria hepatica, Vermeidung eines Reflux, eine intakte Portalzirkulation und grosse Kontrastmittelmengen.

RÉSUMÉ

L'angiographie hépatique faite par injection sélective du moyen de contraste dans l'artère hépatique à raison de 3-5 ml/s est une amélioration de la technique de diagnostic des tumeurs hépatiques et semble aussi utile pour mettre en évidence d'autres lésions hépatiques. Les facteurs essentiels pour le succès d'une angiographie hépatique par injection lente sont le cathétérisme sélectif de l'artère hépatique, l'absence de reflux, un débit portal intact et de grandes quantités de moyen de contraste.

REFERENCES

- | | |
|---|---|
| ALLEN T. Steering device for catheterizations observed in its clinical application. | phyl and some vascular and enzymatic reactions. <i>Am J radiol</i> (1966) Suppl No 260. |
| BARTLEY O, HILLA PER C G R. In demonstration of hepatic angiography. | PERLIN J S. Arterial scintigraphy and angiography. <i>Diagnosis</i> 8 (1969) 161. |
| BOJANOV E. Selective hepatic angiography. <i>Hépat</i> 15 (1963). | primary and secondary tumors of the liver. <i>Rev</i> |

- and ABRAM H. L. Roentgenographic diagnosis of primary carcinoma of the liver. *Acta radiol. Diagnosis* 3 (1965) 257
- LAUDE J. and TILLY U. Angiography in hepatic rupture. *Acta radiol. Diagnosis* 11 (1971) 363
- BIERNAN H. R., BYRON R. L. JR., KELLEY K. H. and GRADY A. Studies on the blood supply of tumors in man. III. Vascular patterns of the liver by arteriography in vivo. *J. nat. Cancer Inst.* 12 (1951) 107
- BRENNER C. and YOUNG G. The blood supply of neoplasms in the liver. *Amer. J. Pathol.* 30 (1969) 1954
- GLICKMAN M. G. and HANDEL S. F. Opacification of hepatic veins during celiac and hepatic angiography. *Radiology* 103 (1972) 565
- HAKKIO I. and LAUDE J. Hepatic angiography enhanced by slow injection technique and tolazolin. To be published
- HEALEY J. E. Vascular patterns in human metastatic liver tumors. *Surg. Gynec. Obstet.* 120 (1965) 1187
- JENSEN R. and LAUDE J. Leverangiografi med låg injektionshastighet (In Swedish) Paper presented at Meeting of Swedish Soc. Med. Radiol. Stockholm Dec. 1971
- LAUDE J. and RIVKIN R. Cholangiocarcinoma. *Radiology* 100 (1971) 573
- and WIRTANEN G. W. Celiac epinephrine enhanced angiography. *Amer. J. Roentgenol.* 110 (1970) 818
- KIRKHAM B. C., TYRON I. B. and WIRTANEN G. W. Comparison of ^{131}I macroaggregated liver scanning and selective hepatic arteriography. *J. nucl. Med.* 11 (1970) 196
- LINDQVIST A. The vascular supply of tumors with special reference to the capillary angio-architecture. *Acta path. microbiol. scand.* 22 (1945) 493
- RUBIN P. H. and CASARETT G. Microcirculation of tumors. Part I. Anatomy, function and neoplasms. *Clin. Radiol.* 17 (1966) 220
- SCHENK Q. G. J., McDONALD J. C., McDONALD K. and DRAPANAS T. Direct measurement of hepatic bloodflow in surgical patients with related observations on hepatic flow dynamics in experimental animals. *Ann. Surg.* 156 (1962) 463
- THOMLSON R. H. and GRAY L. H. The histological structure of some human lung cancers and the possible implications for radiotherapy. *Brit. J. Cancer* 9 (1955) 559
- WATSON R. C. and BALTAXE H. A. The angiographic appearance of primary and secondary tumors of the liver. *Radiology* 101 (1971) 539
- WILLIAMS R. C. and WISE R. E. Infusion hepatic angiography. Assessment of hepatic malignancy via the infusion catheter. *Radiol. Clin. N. Amer.* 8 (1970) 43
- WIRTANEN G. W. Angiographic technique in the diagnosis of liver metastases. Second Congr. EAR, Amsterdam 1971
- Transbrachial hepatic tumor evaluation. 56th Scientific Assembly, RSNA, Chicago, Ill. 1970
- BERNHARDT L. C., MACKMAN S., RAMIREZ G., CURRERI A. R. and ANDERFIELD F. J. Hepatic artery and celiac axis infusion for the treatment of upper abdominal malignancies. *Ann. Surg.* 168 (1968) 137
- and LAUDE J. Epinephrine effect in hepatic, pancreatic and biliary tumor arteriography. VII ICR, Tokyo 1969

CALCIFICATIONS IN METASTASES FROM ADENOCARCINOMA OF THE COLON

P G ROSE

The occurrence of calcification in the secondary deposits of colonic adenocarcinoma is now well recognised but detailed reports of these cases in the literature are uncommon (APPLEBY & HACKING 1958; MIELE & EDMONDS 1963; FRENCH *et al.* 1964).

Two cases are presented which demonstrate pathognomonic radiologic features of concurrent retroperitoneal, hepatic and para-aortic node metastases from adenocarcinoma of the colon. Each case showed urographic features of retroperitoneal metastases that have not to the author's knowledge been previously reported.

Case reports

Case 1. A 36-year-old patient first presented with painless bloodstained diarrhoea but he was otherwise in good health. A family history of polyposis coli was obtained. On examination an ill-defined mass was palpable in the left iliac fossa. Barium enema examination revealed multiple polyps throughout the large bowel and an annular carcinoma in the lower descending colon. No evidence of intra-abdominal calcification was found at that time on survey films.

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Fig. 1 Case 1. Calcified nodes adjacent to the body of L2.

An abdominal perineal resection with total colectomy was undertaken. No local or regional lymph node deposits were detected. There was no calcification either in the gross specimen or on section of the tumour which histologically was an adenocarcinoma of mucoid type.

The patient was discharged and remained symptom free for 18 months when an episode of left sided abdominal pain resulted. His readmission Survey films of the abdomen then showed a calcified oval mass closely related to the body of the second lumbar vertebra (Fig. 1). Urography showed lateral displacement of the left kidney, angulation of the upper ureter and pelviureteric junction together with abnormal pelvic calyceal appearance suggesting extrinsic pressure at the level of the renal hilum. Calcified metastases in the para-aortic nodes and retroperitoneal space were suggested.

Three months later he was admitted for the third time with progressive right loins and left loin pain radiating to the lower abdomen and thigh. Survey films of the abdomen now showed in addition to the calcified para-aortic nodes characteristic miliary calcification over the right lobe of the liver which had not been present previously (Fig. 2). A liver scan using colloidal ^{99}Tc showed a large area of diminished uptake lying anteriorly in the right lobe of the liver corresponding in size and position to the calcification seen on the survey films (Fig. 2b). There was no clinical or radiologic evidence of more extensive dissemination.

A course of radiation therapy to the para-aortic glands resulted in moderate subjective improvement. The patient died at home two and half years after the onset of symptoms.

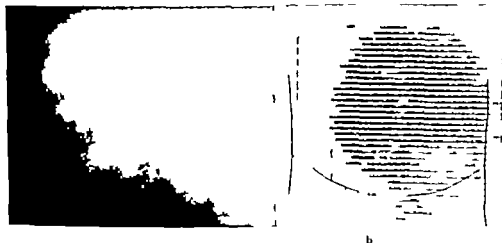


Fig 3 Ca 1 a) Cloud of fine calcification in the liver b) Lateral scan (^{99}Tc) Large area of diminished uptake anteriorly in the right lobe

Ca 2 A 32 year old housewife who first presented to another hospital with the complaint of nausea associated with fat intolerance and non specific right upper abdominal pain. Cholecystography at that time showed normal gall bladder function. Four months later she was admitted to this hospital with history of anorexia and weight loss. There was no other relevant history in particular there was no alteration of bowel habit.

On examination there was tenderness beneath the right costal margin and the gall bladder was thought to be enlarged. The patient had no jaundice and no abnormality as found on rectal examination. Chest film and barium examination of the upper alimentary tract were normal. On survey film for cholecystography several areas of cloud like microcalcification in the liver were found. There was no excretion of Sobu Bilopun. Review of the earlier cholecystogram did not reveal any calcification although the survey films were not technically of the highest quality.

These findings were reported as indicating the presence of metastases the colon being suggested as the most likely primary site (Fig 3). A liver scan demonstrated several areas of absent uptake those in the right lobe corresponding in size and position to the calcification seen on the survey films (Fig 3 b). Barium enema examination showed short annular carcinoma in the distal transverse colon close to the splenic flexure. Urography showed markedly abnormal pelvic cal appearance on the left side slight lateral displacement of the kidney and marked notching of the upper ureter margin. These appearances were attributed to extrinsic compression (Fig 4). Peritoneal metastases were again suggested.

At laparotomy there were multiple nodules throughout the liver retroperitoneal space and omentum. No tumour was seen in the kidney as seen. The pelvis and uterine cervix were normal. The primary lesion was a non-obstructing carcinoma at the splenic flexure for which the patient was operated. As performed. Biopsy specimens from macroscopically involved sites partially necrotic but well differentiated

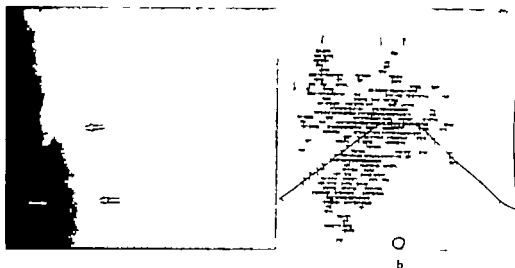


FIG. 3 Case 2 a) Fine calcification in the liver b) Anterior scan (^{99}TcM) Several areas of accumulation of contrast medium in the tumour (\rightarrow)

adenocarcinoma of the cold type. There was no evidence of calcification in the primary lesion nor in the biopsy specimens.

All films were reviewed: no other intra-abdominal calcification was observed and there was no clinical or radiologic evidence of extra-abdominal dissemination. The patient was eventually discharged but deteriorated progressively and died at home 10 months after the onset of symptoms.

Discussion

In a review of the literature some 25 examples of calcification in the hepatic metastases from colonic adenocarcinoma have been found. The presence of calcification in local and distant deposits other than the liver is still less common, there being fewer than 10 well-documented examples (McNair & Trapnell 1971; Ghahremani & Straus 1971; Govoni & Alcantara 1968). Calcification and even ossification has been reported on rare occasions in the primary tumour (Green 1959; Fletcher et al. 1967). No reference to abnormal urographic appearances has been found.

The detection of microcalcification is dependent on the application of suitable radiographic technique. This feature of colonic carcinoma may be identified before the development of symptoms indicative of large bowel disease and should lead to a detailed assessment of the lower alimentary tract and a search for calcification or other evidence of more extensive spread. The two cases presented show the particular value of urography in this respect.



Fig 4 Case Urography left ureteric defect on left side Normal right side

Hepatic calcification The stippled intrahepatic calcification has in the past been regarded as pathognomonic of colonic particularly rectosigmoid, adenocarcinoma (MIELE & EDWARDS) but liver calcification has also been reported on rare occasions in such metastases from the stomach (JAEDE & BRUNN, 1963) the breast (SAGHATOESLAMI et coll 1962) malignant melanoma and following radiation therapy for bronchial adenoma and malignant salivary tumour (FRED et coll). In all these the calcification has been of variable distribution but nodular coarsely granular or shell like in type. The secondary deposits of ovarian cystadenocarcinoma are commonly widespread within the liver cavity and contain fine psammoma granules.

The calcific residues of granulomatous infection or parasitic infestation are usually readily identified by the distribution and localisation of deposits, from evenly distributed miliary calcification in tuberculosis, brucella infection, plasma leishmaniasis to the gross curvilinear and plaque like calcifications in echinococcus cysts and intrahepatic abscesses. The rare cases of calcification of the liver have shown gross irregular concretions with sharp demarcation from the adjacent liver parenchyma (KARRAS et coll).

Calcification is also known to occur in primary malignancy and its appearance and distribution differs from that seen in metastases. Cavernous haemangioma characteristically shows calcification in the form of central whorls and ring like clusters (PLATT, 1962). Pleomorphic adenoma has a heavily pitted mottled appearance, whilst the earliest appearance may be seen like a pecked way (HADDON & KEMP HARRIS, 1962). With calculi in the dilated ducts (KARRAS et coll).

SUMMARY

TWO cases with evidence of concurrent hepatic, para-aortic and retroperitoneal metastases from mucin-secreting adenocarcinoma of the colon on survey films of the abdomen and tomograms are presented. The features mentioned are considered to be pathognomonic of the organ of origin and the histological appearance of these tumours. The relevant literature and differential diagnosis of individual features is discussed.

ZUSAMMENFASSUNG

Zwei Fälle bei denen gleichzeitig Leberrnetastasen paraaortal gelegene und retroperitoneale Metastasen von einem Mucin sezernierenden Adenocarcinom des Kolon auf Übersichtsaufnahmen des Abdomen und Urogrammen nachweisbar waren, werden beschrieben. Dieses Erscheinungsbild wird als pathognomonisch für das Ursprungsorgan und das histologische Bild dieser Tumore betrachtet. Die einschlägige Literatur und die Differentialdiagnose der individuellen Erscheinungsbilder werden diskutiert.

RÉSUMÉ

Présentation de deux cas dans lesquels les radiographies d'ensemble de l'abdomen et les tomographies montraient des signes de métastases hépatiques para-aortiques et rétroperitoneales simultanées d'un adénocarcinome mucosécrétant du colon. Les caractères décrits par les auteurs sont considérés comme pathognomoniques de l'organe d'origine et de l'aspect histologique de ces tumeurs. Les auteurs examinent la littérature et le diagnostic différentiel de chacun de ces signes.

REFERENCES

- APPELBY A. and HACKEN P. M. Calcification in hepatic metastases. *Brit J Radiol* 31 (1958) 449.
- CALAPPA S., BONADONNA G., UELINGH C. and VIERONNI U. Lymphangiography in the diagnosis of retroperitoneal node metastases in rectal cancer. *Brit J Radiol* 40 (1967) 584.
- FLETCHER B. D., MORRIS C. L., CHRISTIAN W. H. and BROGDON B. G. Calcified adenocarcinoma of the colon. *Amer J Roentgenol* 101 (1967) 301.
- FRIED H. L., EISAND J. M. and COLLIER L. C. Calcifications in intra abdominal and retroperitoneal metastases. *Amer J Roentgenol* 91 (1964) 138.
- GRANDERMAN G. G. and STRAUSS F. H. Calcification of distant lymph node metastases from carcinoma of colon. *Radiology* 99 (1971) 63.
- GOVONI A. F. and ALCAANTARA A. N. O infying metastatic carcinoma of the colon. *Amer J Roentgenol* 104 (1968) 561.
- GREEN G. J. Calcification in carcinoma of the colon. *J Fac Radiol* 10 (1959) 219.
- HADDOW R. A. and KELLY HARPER R. A. Calcification in the liver and portal system. *Clin. Radiol* 18 (1967) 225.
- JALDEK W. and BERLINER D. Calcification in liver metastases from gastric carcinoma. *Fortschr Röntgenstr* 98 (1963) 54.
- KARRAS B. G., CANNON A. H. and LARSEN B. Hepatic calcifications. *Acta radiol* 57 (1962) 458.

In the two cases presented here the calcifications were extremely fine and consisted of a cloud like distribution of minute granules fading at the margins into apparently normal liver substance. This detail could only be observed on film of the highest quality. Reproduction of the fine detail and contrast gradations of the originals has proved difficult.

Retropertitoneal metastases A search of the literature suggests that radiologically detected metastases from these tumours are rare. It seems likely that such deposits are more frequent than is commonly believed but their site and distribution lead either to failure of identification or to misinterpretation. The importance of comparison with previous films must be emphasised. The elimination of confusing calcification in adjacent structures can usually be achieved by careful positioning of the patient but recourse to tomography may be necessary. In Case 1 readily identifiable calcification developed over a period of 18 months in the position of the para aortic nodes very similar to that shown in the necropsy specimen of the case reported by STEINL (1967). In Case 2 there was a much shorter interval between the onset of symptoms and detailed assessment which probably precluded the possible development of radiologically detectable calcification in the lymph nodes. Retropertitoneal extension of the tumour mass was indicated by the urographic findings and subsequently confirmed both surgically and histologically.

A large number of tumours can metastasise to the para aortic nodes and retropertitoneal space but calcification in them is extremely rare. McNAM & TRAPNELL quoted only one example of mucin secreting adenocarcinoma of the stomach. The para aortic group of nodes has been shown to be a site of predilection for the secondary deposits of colonic, particularly recto sigmoid carcinoma in the lymphangiographic examinations of CHIAPPA et coll (1967).

The factors governing the development of calcification in such tumours are uncertain. The presence of devitalised tissue surrounded by normal parenchyma is associated with a low carbon dioxide tension that encourages calcium deposition but BATLAN (quoted by GREEN 1959) suggested that the high proportion of mucinous material in these tumours might function as an exchange matrix.

It is suggested that the appearance of typical calcification in these sites is pathognomonic of mucin secreting adenocarcinoma of the colon.

Acknowledgements

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ANGIOGRAPHY IN INTESTINAL CARCINOID

R BJORN HANSEN and T AALHUS

The first report on the angiographic signs of carcinoid of the bowel was presented by REUTER & BOJSEN in 1966. These authors listed stellate arterial appearances, narrowing of deep mesenteric branches, poor to moderate accumulation of contrast medium in the tumour and non filling of veins in two cases. A perusal of the literature revealed only three more cases of the intestinal carcinoid syndrome submitted to angiography (BARD et coll. 1966; SHIMAKI et coll. 1971; CLAPS et coll. 1972). Due to the rarity of this tumour and the few angiographic reports it was thought that it might be of interest to publish four cases subjected to angiography at this centre.

Case reports

Case 1. Male, aged 60 years who for 3 years had had attacks of flushing and diarrhoea and for one year dyspnoea. The heart was enlarged with tricuspid regurgitation on catheterization. A tumour the size of an egg was present in the distal part of the ileum with possible infiltration of the caecum at the laparotomy. Barium meal examination

Angiography of the terminal branches of the mesenteric arteries in the ileum (Fig. 1) showed an irregular calibre of the caecum as well as of the ileal area as relatively band-like as of the irregular caecum. The newly

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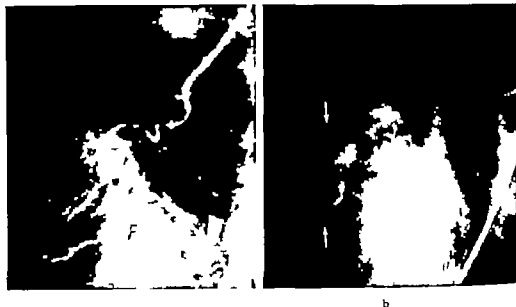
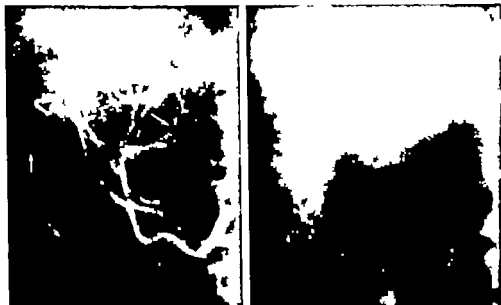


Fig. 1. Case 1. Angiography of the superior mesenteric artery. a) Arterial phase. Irregular calibre and tortuous course of the ileocolic artery and its branches. b) Parenchymal phase. Accumulation of contrast medium in the tumour (→).



Fig. 2. Case 2. Angiography of the superior mesenteric artery. Arterial phase. The distal part of the superior mesenteric artery (→) as well as the proximal part of the ileocolic artery (↔) are much narrowed. The ascending colon, caecum and the terminal ileum are mainly supplied from the middle colic artery through the widened marginal artery. A definite tumour mass is visible. Irregular calibre and course of the branches to the terminal ileum from the anastomosis between the ileocolic and superior mesenteric arteries (↔→) (subtraction).



b

Fig. 3 Case 2 Angiography of the celiac artery. a) Arterial phase Expansion of the liver with circumferential displacement of hepatic branches (→) b) Parenchymal phase Accumulation of contrast medium in multiple metastases in the liver

formed tumour nodule. Accumulation of contrast medium in the tumour was evident in the parenchymal phase. The angiography also revealed metastases in the liver and the operation neoplasm in the terminal ileum was involving the caecum in accordance with the angiographic findings. The tumour infiltrated the mesentery of the terminal ileum and had also invaded lymph nodes in this region. A large tumour and several smaller nodules were palpated in the liver.

Histologic examination revealed a carcinoid tumour. The course was uneventful and the patient remained well at the control three months later.

Case 3. Female, aged 47 years who for several years had had some diarrhoea and for 5 years attacks of flushing. Cyanosis and pellagra like exanthema had developed in the last two years. A systolic murmur was compatible with insufficiency of the tricuspid valve. A markedly increased level of 5-hydroxyindoles etc. acid was present in the urine. Conventional barium meal and enema examinations failed to reveal any signs of malignancy.

Angiography of the superior mesenteric artery disclosed considerable narrowing of the lower part of this artery as well as the ileocolic artery. The distal ileal arteries were filled mainly through dilated marginal arteries of the middle colic artery. Some of the anastomoses arising from the distal ileocolic artery to the terminal ileum were irregular in calibre (Fig. 2). Angiography of the hepatic artery disclosed expansion of the right hepatic lobe with circumferential displacement of the arteries around them (Fig. 3). No abnormal nodules were evident. Accumulation of contrast medium appeared in the tumours in the parenchymal phase.



Fig. 4. Case 2. Hepatic phlebography. Injection into a vein of the left lobe demonstrates compression of its proximal part and collateral emptying into a major vein in the right lobe.

Phlebography of the left hepatic vein (Fig. 4) demonstrated its proximal compression with collateral veins coursing from the left to the right lobe.

Ligature of the hepatic artery was planned but had to be abandoned due to the poor general condition of the patient.

Case 3. Female, aged 49 years, who for four years had had attacks of flushing, tachycardia and diarrhoea. A considerably increased level of 5-hydroxyindoleacetic acid was present in the urine. No abnormality was detected by barium meal or enema examinations.

Angiography of the superior mesenteric artery revealed considerable irregularity of calibre and course of the superior mesenteric and ileocolic arteries distally. The latter were almost occluded and the corresponding area of supply was filled in a considerably dilated marginal artery between the middle colic and the superior mesenteric arteries (Fig. 5). The arterial appearances suggested that the ileum was crowded in the right iliac fossa; the small arteries in this region lay in a radiating formation. No signs of secondary deposits in the liver were detected by angiography of the celiac artery. Operation revealed a tumour in the ileum one metre proximal to the ileocaecal valve and spreading into the mesentery and lymph nodes. A few small hepatic metastases were palpated.

Histologic examination revealed a carcinoid tumour.

Case 4. Female, aged 58 years, who for one year had had increasing diarrhoea considered to be due to malabsorption with increased excretion of fat. A barium meal examination suggested enteritis and no malignancy was detected. A poorly defined mass was palpated on the right side of the abdomen. A specimen obtained by needle biopsy of the liver contained malignant tissue compatible with carcinoid.

Angiography of the superior mesenteric artery demonstrated markedly irregular narrowing of its lower part. The artery was wide and tortuous and gave off radiating branches (Fig. 6). Subsequent urine analysis disclosed an increased level of 5-hydroxyindoleacetic acid. Marked ascites and oedema of the lower extremities gradually developed and no operation was considered possible.



Fig 3 Case 3 Angiography of the superior mesenteric artery. Arterial phase. The ileocolic artery (→) and distal part of the superior mesenteric artery irregularly narrowed. The intestinal and peripheral branches supplying the distal ileum run in a radiating fashion and the corresponding terminal arcade has tortuous course.

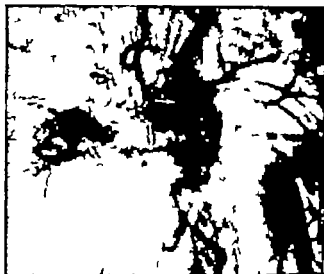
Discussion

The carcinoid tumour is rare even if it represents the majority of the small bowel tumours (MARSHALL & LINDNER 1970). The intestinal carcinoid usually arises in the appendix although it may occur in the ileum and less commonly in other parts of the gastrointestinal tract. The tumour grows slowly constricting the bowel and invading the mesentery. Its tendency to spread as well as the production of secretions seem to vary with the site of origin.

The carcinoid of the appendix rarely metastasizes while those arising in other regions of the gastrointestinal tract tend to spread to the liver, regional lymph nodes, lungs and bones (ROBBINS 1967). Carcinoids of the ileum and appendix secrete 5-hydroxytryptamine (serotonin) while those of the colon and rectum practically never have any secretory activity (ANTHONY & DAUKY 1970).

When invading the mesentery the tumour elicits a marked fibroplastic activity. This causes retraction of the mesentery and crowding of the bowel in a tangle around the tumour. Hence upon dissection a tangle of the vessels of the mesentery is also exerted by the tumour. This is referred to the direct encasement of vessels by malignant extending lymphatics (REUTER & BOJSEN

Fig. 6 Case 4. Angiography of the superior mesenteric artery. Arterial phase. The lower part of the superior mesenteric artery is irregularly narrowed (\rightarrow) with the wide and tortuous terminal part (\rightarrow) partly filled through an irregular arcade from the lower intestinal artery. The peripheral vessels in this region have a radiating appearance (subtraction).



1966). However, investigations by ANTHONY & DRURY (1970) indicated that this may be an elastic sclerosis of vessels in the mesentery elicited by the secretions. The changes in the right heart valves are also generally considered to be caused by pharmacologic substances brought with the blood stream from the primary lesion (McHUSICA 1956). The exact nature of these active substances has not yet been established. Changes in Cases 2, 3 and 4 were most evident in mesenteric vessels distant from the primary growth, even if the angiographic demonstration of the tumour itself might have been questioned.

The few cases hitherto reported present strikingly similar angiographic appearances characterized by a radiating course of the vessels and irregular narrowing of even larger vessels in the vicinity of the tumour. A slight to moderate accumulation of contrast medium in the tumour in the parenchymal phase with absent or poor venous filling are also almost always evident.

The angiographic appearances of the hepatic metastases are however not specific. The metastases in the present material were disclosed by a circumferential displacement of hepatic arterial branches, and by a moderate accumulation of contrast medium in the parenchymal phase. As in one case the signs may be so slight as to escape notice. NESEBAR *et coll.* (1966) and LUDVIG *et coll.* (1966) reported however high vascularity and marked accumulation of contrast medium in carcinoid liver metastases, changes that were confirmed by BRUNO MARA *et coll.* (1970).

Other conditions causing crowding of the bowel may simulate carcinoid tumours angiographically. LUNDERQUIST & LUNDERQUIST (1968) demonstrated

changes in the vascular course associated with peritoneal adhesions and AARJUS (1971) described the angiographic appearances in cases of closed loop strangulating obstruction. A crowding of the bowel and radiating course of the vessels may then be demonstrated even irregularity of the vessels by compression kinking or spasm may occur.

It should be remembered that a carcinoid may cause peritoneal adhesions (HORSLEY & BAHR 1970) and may thus be associated with adhesions producing attacks of intestinal obstruction. This adds to the difficulty in the angiographic differentiation between a carcinoid tumour and other conditions resulting in adhesions and small bowel obstruction. A history of attacks of flushing may then be decisively important. GOLD & REIDMAN (1972) in a recent publication also stated that a similar arterial arrangement may be evoked by sclerosing fibrous peritonitis referable to the marked fibrotic reaction in this condition. The angiographic features associated with an intestinal carcinoid possibly therefore represent a type of abnormal process rather than a specific entity.

SUMMARY

Four cases of carcinoid of the bowel are presented and the angiographic features described in detail. Both the primary tumour and its metastases usually evoke distinct angiographic changes. The appearances are discussed against the background of the mode of growth and spreading of the tumour as well as of its secretory activity. Some differential diagnoses are considered.

ZUSAMMENFASSUNG

Vier Fälle von carcinoiden Tumoren des Darms und deren angiographische Befunde werden beschrieben. Sowohl der Primärtumor als auch dessen Metastasen produzieren typische Bilder. Die Erscheinungsformen werden mit der Pathologie des Tumors und seiner Ausbreitung und mit seiner sekretorischen Aktivität in Bezug gebracht. Die Differenzialdiagnose wird besprochen.

RÉSUMÉ

Les auteurs présentent 4 cas de carcinoides intestinaux et décrivent en détail leurs aspects angiographiques. La tumeur primitive et ses métastases ont habituellement des signes angiographiques distincts. Les images sont étudiées en fonction du mode de croissance et de la dissémination de la tumeur ainsi que de son activité sécrétoire. Les auteurs étudient certains diagnostics différentiels.

REFERENCES

- AARJUS T. Angiography in acute mechanical obstruction of the small intestine. *Acta radiol* (1971) Suppl. No. 306.
- ARMSTRONG P. P. and DICKINSON R. A. Flushing attributable to mesenteric blood vessels in angiodysplasia. *Br J Surg* 58: 23 (1970).

- BARD M, BÉVUTH V, PALGAN B, TURIAU J D et BOUDRON R. Tumeur carcinoïde du caecum. Intérêt de l'artériographie mésentérique. *Sem Hop Paris* 42 (1966) 1144.
- BENGMARK S, ALMJO O, HANSTRÖM L and ROSENBERG C. The reliability of celiac angiography in diagnosing liver tumours. *Bull Soc Int Chir* 29 (1970) 133.
- CLAPS R J, LAUDE A, LILIENTHAL R and MISZA M. Angiographic demonstration of an ileal carcinoid. *Radiology* 103 (1972) 87.
- GOLD E R and REDMAN H C. Mesenteric fibrosis simulating the angiographic appearance of ileal carcinoid tumor. *Radiology* 103 (1972) 85.
- HORSLEY B L and BAUER R R. Fibroplastic response to intestinal carcinoid. *Amer Surg* 36 (1970) 676.
- LUDT H, FAIRLANDER H J und RENOLDI I. Zur Darstellung von Karzinoid Lebermetastasen mittels mesenterischer Arteriographie. *Schw med Wochr* 96 (1966) 1642.
- LUNDENQUEST A and LUNDENQUEST A. Arteriographic appearance of intestinal adenomas. *Amer J Roentgenol* 103 (1968) 354.
- MARRHAS R H and LINDER A E. *Radiology of the small intestine* p 315. W B Saunders Co Philadelphia 1970.
- McKINCKY V A. Carcinoid cardiovascular disease. *Bull Johns Hopk Hosp* 98 (1956) 13.
- NEHERAR R A, POLLARD J J and STONE D L. Angiographic diagnosis of malignant disease of the liver. *Radiology* 86 (1966) 284.
- REITER S R and BOTJEN E. Angiographic findings in two ileal carcinoid tumors. *Radiology* 87 (1966) 836.
- ROBBINS S L. *Pathology*. Third edition. W B Saunders Co Philadelphia London 1967.
- SHIMKIN P M, DE VITA A T and DOFFMAN J L. Arteriography of an ileal carcinoid tumor. *J Canad Ass Radiol* 22 (1971) 259.

USE OF IODINE CONTAINING POLYMERS FOR CALIBRATION AND ABSORPTION MEASUREMENTS IN RADIOGRAPHY

B. LANTZ and E. SORVÉN

Small absorption changes in the roentgen relief caused by the passing of an iodine contrast medium in a selected area of the fluoroscopic image provide the basis for videodensitometric blood flow measurements. If quantitative data on blood flow are to be based on the dispersion of a contrast medium injected into the circulation a careful calibration of the densitometer has to be performed for different dilutions of the iodine contrast medium.

The usual method of calibrating the detector system for known amounts of contrast media is experimentally in practice timeconsuming and expensive because of the instability of the contrast medium. Furthermore, it is necessary to use some kind of calibration material with a certain degree of absorption.

Consequently we have tried to develop a calibration method based upon a solid radiation stable material containing iodine, easy to mould into exact dimensions and easy to provide with the iodine content desired.

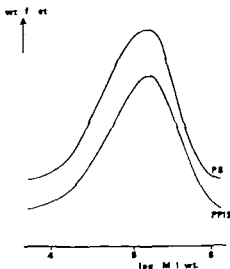


Fig. 1. Molecular weight distributions of polystyrene (PS) and iodinated polystyrene (PPIS). Measurement by GPC according to ANDERSON & SORELL.

Solid iodine-containing materials

Mouldable materials from potassium iodide and some kind of binder e.g. paraffin wax were prepared. However it proved rather difficult to obtain a homogeneous material in this way. Instead of potassium iodide we also tried iodide saturated anionic exchangers.

Further other methods were tried such as dissolving elementary iodine into polymers already moulded into their final shape, like plates of poly (methyl methacrylate), PMMA and polystyrene, PS. No change in the iodine content of these materials could be observed after storage in air for several days at 120°C. The adjustment of the iodine content to a suitable value was somewhat difficult to carry out with these methods. Also it is necessary to consider the risks of losing iodine by migration when the calibration material is kept in contact with other plastic products for a longer period of time.

The best results were obtained by chemical bonding of iodine to a high polymer. Thus iodine was introduced into polystyrene (PS) by means of aromatic substitution. In this way poly (p-iodine styrene) (PPIS) is formed in a high yield.

Iodinated polystyrene, PPIS

Synthesis of poly (p-iodine styrene) (PPIS) In this synthesis originally suggested by BRAUN (1959) sulphuric acid acts as a catalyst and the iodic acid as an oxidizing agent for the hydrogen iodide formed.

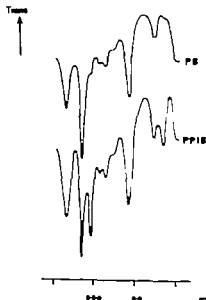
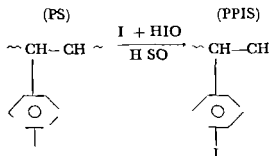


Fig. 2 Infrared spectra of polystyrene (PS) and iodinated polystyrene (PPIS) KBr tablets



The synthesis was carried out in a glass reaction vessel 2 litre in volume with a stirrer and reflux condenser. Fifty-two g of granulated PS was dissolved in 1500 ml of nitrobenzene at room temperature while being stirred. Fifty-one g of iodine crystals (subl. P.A.) was then added and dissolved and to this was added 19 g of iodic acid (P.A.) for the oxidation of the hydrogen iodide formed. Then 50 ml carbon tetrachloride was added so as to bring back sublimated iodine from the condenser to the reaction mixture. Finally 100 ml of sulphuric acid 50 wt % was added as a catalyst. The mixture was heated to 90°C. The mixture was kept at this temperature for 2 hours while being stirred vigorously. Then it was allowed to cool off. Nitrobenzene was added to improve precipitation and the mixture was slowly poured out into 15 litre of methanol while the polymer thus precipitated was somewhat

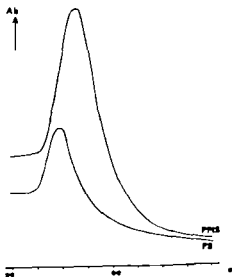


Fig. 3. Ultraviolet spectra of polystyrene PS (10 g/l) and iodinated polystyrene PPIS (5 g/l) Chloroform solution.

discoloured by free iodine. This was removed by successively adding solid sodium bisulphite altogether about 1 g until no further reduction in colour could be observed.

The precipitate was then washed 5 times by suspending it in 2 litre of methanol and finally with 2 litre of methanol on the suction filter. The precipitate was dried at room temperature in an exsiccator until constant weight was reached. The final product was 93 g of a cream white fine grained powder. No degradation of PS occurred during the reaction (Fig. 1). As shown in Figs 2 and 3 the iodination of PS resulted in PPIS. The degree of conversion was 91% (Table 1).

Standardizing the iodine content. The iodine content and the radiation absorption of PPIS are much too high for direct use as a calibration substance. By means of coprecipitation with PS from a solution in tetrahydrofuran (THF) a homogeneous polymer mixture with an appropriate iodine content could be prepared. The mixture was made on a volume basis of PPIS:PS = 1:15. The density of the polymers used was determined by weighing moulded plates of known dimensions. One part by volume of PPIS = 9.65 g density 1.75 and 15 parts by volume of PS = 78.75 g density 1.03 were dissolved in 1 litre of peroxide free (ANDERSSON & SORVILK 1971) THF and precipitated into 7 litre of methanol. The precipitate was sucked up and dried at room temperature.

Methods of analysis. IR and UV spectrometry (Beckman IR 9 and Beckman DK 2) was used to make sure that the iodination had resulted in poly (p-iodine

Table 1
Analysis of iodinated polystyrene (PPIS)

Element	Found (wt %)	Theoretical (wt %)	Calculated conversion (%)
C	44.4	44.9	92
H	3.4	3.5	91
I	50.4	50.7	91

Table 2
Analysis of mixture of iodinated polystyrene and polystyrene (PPIS-PS) 1:15

PPIS+PS (1:15)	Iodine content (wt %)
Untreated	6.7
Röntgen irradiated	6.8
UV irradiated	6.6

ene) (see further Figs 2 and 3 and compare with spectra in BRAUN and VOST ET AL.) The chemical composition was determined by ultra micro elementary analysis (Tables 1-2).

The molecular weight distribution for the PS used and the final product PPIS was determined by means of gel chromatography (GPC) using a Water GPC Model 200 and THF as solvent. For experimental details and calculations see DERASOV & SOMOVA.

Moulding of plates Plates of PS, PPIS and PPIS + PS (1:15) were compression moulded at 10^4 kP/cm² (14.2×10^4 p.s.i.) with a moulding cycle of 5 minutes. Thin plates were moulded at room temperature, plates thicker than 1 mm at 130°C. This thermal treatment did not cause any visible discolouration of the plates. Thick plates (100 mm diameter) were moulded to oversize and then surface ground to the thickness required. For other plates the thickness desired was obtained directly at the moulding process by adjustment of the polymer quantity and the moulding pressure. For all plates the plates were heated for 5 minutes at 135°C. The following thicknesses were obtained: 1, 2, 4, 6, 8, 10, 12, 15, 20 mm.

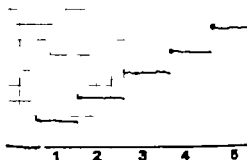
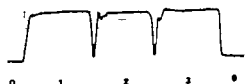


Fig. 4. The iodine content in each plate of step wedge measured by a logarithmated videodensitometer. The linear amplitudes indicate the linearity of the instrument.

Fig. 5. One volume unit of 10 mm high moulded plate (71.9 mg I/ml) is compared with the same volume of two separate dilution series of Isopaque cerebral (Nyegard). Dilution 1:6 (46.7 mg I/ml) in the two series marked 1 and 3 in the figure gives the same amplitude as the moulded plate 2.



Stability tests. The resistance to roentgen of 2 mm plates of PPIS + PS (1:15) was tested at a distance of 46 mm from the wolfram anticathode of a diffraction tube (Philips PW 2074/65) for 130 minutes at 54 kV and 18 mA. The exposure was calculated to be about 500 000 R. This treatment gave rise to a yellow brown discolouration of the surface layer of the plates due to liberation of free iodine. But there were no signs of iodine diffusing out of the plates according to the elementary analysis (Table 2).

The resistance to UV and visible light was determined by means of exposure for 75 hours in a Xenotest apparatus. A faint discolouration of the surface layer could be observed but no appreciable change in iodine content or radiation absorption (Table 2).

The use of the solid polymer for calibration in videodensitometry. A step wedge of plates of iodine polystyrene (cf. LANTZ & STRID, Fig. 3) is examined by a logarithmated videodensitometer in television fluoroscopy with fixed tube voltage and current as described by LANTZ. The iodine content in the different steps had the proportions 1:2:3:4:5 in accordance with the measured result in Fig. 4.

The thickest plate in this series 10 mm high is compared with dilution of a known contrast medium of the same height. As seen in Fig. 5 the absorption of the plate is equivalent to a dilution of Isopaque cerebral (Nyegard) 1:6. The

iodine content per volume unit of the plate and the dilution is 71.9 mg/ml respectively 46.7 mg/ml. This discrepancy depends on absorption differences between the two solvents i.e. PS and water.

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SUMMARY

By mixing solutions of PS and PPIS and then precipitating the polymer mixture it is possible to obtain homogeneous solid materials with suitable and constant iodine content. It is then easy to mould calibration plates into the shape desired by means of the usual plastics processing methods without any decomposition of the polymer. The material has satisfactory radiation stability and resistance to light. The plates are easier to handle than dilution series of a water soluble contrast medium and are recommended for calibration purposes and absorption measurements of iodine.

ZUSAMMENFASSUNG

Durch Mischen von PS und PPIS Lösungen und nachfolgender Fällung der polymeren Mischung ist es möglich ein homogenes festes Material mit einem geeigneten und konstanten Jodgehalt zu erhalten. Es ist dann einfach Kalibrierungsplatten von gewünschter Form mit gewöhnlichen Plastikbearbeitungsmethoden zu formen ohne das Polymer zu zerstören. Das Material hat eine zufriedenstellende Strahlens- und Lichtresistenz gegenüber Licht. Die Platten sind leichter zu handhaben als Verdünnungsreihen eines wasserlöslichen Kontrastmittels und werden für Kalibrierungsverfahren und Absorptionsmessungen von Jod empfohlen.

RÉSUMÉ

Il est possible d'obtenir un matériau solide contenant une proportion convenable et constante d'iode en mélangeant des solutions de PS et PPIS et en précipitant le mélange. Il est ensuite facile de mouler les plaques d'étalonnage de la forme désirée en utilisant les méthodes habituelles de travail des plastiques sans aucun décomposition du polymère. Cette matière a une stabilité satisfaisante aux rayonnements et une résistance à la lumière. Ces plaques sont plus faciles à manipuler que les séries de dilutions d'un milieu de contraste hydro-soluble et sont recommandées pour l'étalonnage et pour les mesures d'absorption d'iode.

REFERENCES

- ANDERSSON K. and SORVIL E. Thermomechanical degradation of poly (vinyl Chloride) J Polym Sci Part C 33 (1971) 247
- BRAT D. Über Umsetzungen an Poly p lithiumstyrol I Mitt. Darstellung und Hydrolyse der makromolekularen metallorganischen Verbindung Makr Chemie 30 (1959) 83
- LANTZ B. A methodologic investigation of roentgen videodensitometric measurement of relative flow. To be published as a supplement to Acta radiol.
- YANARI S. S. BOVEY F. A. and LAUREY R. Fluorescence of styrene homopolymers and copolymers Nature 200 (1963) 243

TRANSABDOMINAL ROENTGENOLOGIC AND SCINTIGRAPHIC LYMPHOGRAPHY OF THE VENTRAL MEDIASTINUM WITH THOROTRAST AND $^{99}\text{Tc}^{\text{m}}$ S COLLOID IN THE RABBIT

L R GORANSON K JOHANSSON and T OLIN

Lymphatic structures in the pelvis and retroperitoneal space may easily be examined by direct lymphography following cannulation of a peripheral lymph trunk and introduction of a contrast medium. Although examination of the parasternal lymph vessels from the diaphragm and draining nodes is of particular importance in possible malignant infiltration of the breast in for example carcinoma of the medial quadrants the vessels are almost impossible to cannulate. They may however be demonstrated in animals by indirect lymphography after injection of Thorotrast into the peritoneal cavity (BARER 1961 BROVELLI & DOLFINI 1961 ERSKIND 1940 HELD 1932 MENVILLE & ABE 1932 OLIN & SALDEEN 1964 ULLMANN & FRANZ 1934). The main pathway for resorption of large molecules or particles in the peritoneal cavity is via the lymph vessels

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Table 1

Survey of the experiments Number of animals

		N agent	Hyalase	PPP
Thorotrast group I	Selective	4	3	—
	Non selective	3	4	2
⁹⁹ Tc-S group II	Selective	3	2	2
	Non selective	3	3	2

of the diaphragm to the parasternal lymph trunks and nodes in the upper ventral aspect of the mediastinum (SALDEEN 1963)

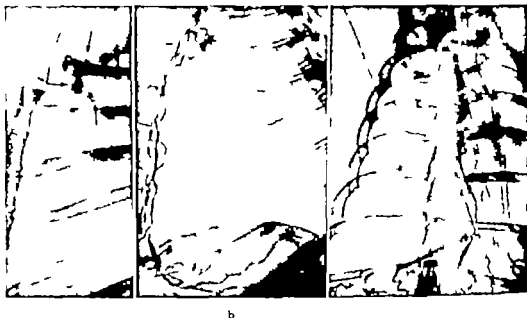
The purpose of the investigation was to clarify (1) whether the deposition of contrast medium (Thorotrast) directly under the diaphragm enhances filling of the parasternal lymph trunks as compared to non selective injection into the peritoneal cavity (2) whether intraperitoneal administration of ⁹⁹Tc-S colloid followed by imaging with a gamma camera gives diagnostic information similar to indirect lymphography with Thorotrast, (3) whether Thorotrast and ⁹⁹Tc-S colloid cause obstruction of lymph vessels, and (4) whether it is possible to increase or decrease the resorption of Thorotrast and ⁹⁹Tc-S colloid by injection of hyaluronidase and polyphlorein phosphate, PPP respectively

Material and Methods Thirty-one Swedish Land rabbits weighing between 1.5 and 3.0 kg were anaesthetized with intravenous pentobarbitone sodium (Mebumalnatium ACO) and in 16 animals (group I) 3 ml Thorotrast (Testagar & Co) were injected into the peritoneal cavity (Table 1). The injection in 4 of these animals was made selectively in the subdiaphragmatic region through a small catheter (OPP 10 OD/ID 0.65/0.25 mm Portex) in 3 animals non selective injection was made in the caudal part of the peritoneal cavity via a venflon cannula (L 120 Viggo) inserted through a small cutaneous incision following local anaesthesia with subcutaneous mepivacaine (Carbocain 1% Bofors Nobel Pharma). For the selective injection the catheter was advanced through a venflon cannula and carefully placed below the diaphragm with the aid of a fine guide wire under fluoroscopy. In 7 animals 100 IU hyaluronidase (Hyalas, Leo) were injected immediately before the contrast medium the technique being selective in 3 and non selective in 4 rabbits. In 2 animals 30 mg polyphlorein phosphate PPP (Leo) were injected immediately before the contrast medium and in these only the non selective technique was used.

Table 2
Results after intraperitoneal Thorotrast

		No of animals	Demonstration time in hours	
			Parasternal lymphatics	Ant mediast nodes
Non selective	No drug	3	2	1
	Hyalase	4	3	0.5
	PPP	2	24	1
Selective	No drug	4	1.5	0.5
	Hyalase	3	2	0.5

Each animal was placed in a prone position following fluoroscopic monitoring of the injection of Thorotrast. Whole body roentgenograms were taken in pa and lateral projections at half hour intervals for two hours hourly for the next 4 hours and at 24 and 48 hours. Exposure factors were 70 to 80 kV 3.2 mA and 0.04 seconds 0.1 mm focus and fourfold direct magnification. Careful collimation and high definition screens (Ruben, Siemens) were used. In a second group (group II) of 15 rabbits 400 μ Ci $^{99}\text{Tc}^m$ S colloid in about 4 ml solution prepared according to PERSSON & NAVERSTEN (1970) were injected intraperitoneally by the selective and non selective techniques similar to those described for the Thorotrast injections in group I. With the selective technique 2 animals received 100 IU hyaluronidase and 2 polyphlorein phosphate (30 mg) before the colloid. With the non selective technique 3 animals received 100 IU hyaluronidase and 2 animals polyphlorein phosphate (30 mg) before the colloid with each technique 3 animals were given the colloid without previous injection of any pharmacologic agent. Before introduction of the colloid a small amount of water soluble contrast medium (Isopaque Cerebral, Nyco A/S) was injected to check the catheter position by fluoroscopy. Each animal was then placed prone under a 4000 channel collimator of a gamma camera (Nuclear Chicago Pho/Gamma III) and the injection performed. Uptake was continuously monitored and recorded at 0.5 min intervals with the Intertechnique digital scintigraphy system (Image digitizer Ca 26 a main memory Tridac BA 110 F 01 a circuit analyzer KB 163 a transfer unit KB 120 and an Amp. 71 Z 19 transfer unit taperecorder). Activity distribution in all animals was recorded for a period of one hour and the distribution in one rabbit followed for 6 hours. A further procedure was carried out in 2



b

Fig. 1. a) Lateral view of chest of rabbit one hour following the intraperitoneal injection of 3 ml Thorotrast. The lymph nodes in the upper anterior mediastinum are filled (\rightarrow). b) After 24 hours. Good filling of the lymphatics parasternally and in the diaphragm. c) A projection

of the animals in group II. In one an intraperitoneal injection of 3 ml of Thorotrast was given 2 days following the first $^{99}\text{Tc}^{\text{m}}$ S collod injection and in the other, which had been injected intraperitoneally with Thorotrast $^{99}\text{Tc}^{\text{m}}$ S collod was administered after an interval of 2 days.

Results

Lymph nodes in the upper anterior mediastinum were demonstrated within half an hour in all animals following the intraperitoneal administration of Thorotrast, except in those that had been injected non selectively and without hyaluronidase and in those with prior injection of polyphloreitin phosphate (Table 2). The uptake of contrast medium in the lymph nodes increased gradually. After 1.5 to 3 hours the parasternal lymph vessels adjacent to the lymph nodes became evident. This was followed by a gradual display of the lymph trunks in a caudal direction until after 24 hours complete end-to-end filling of vessels from the diaphragm to the upper ventral lymph nodes was evident (Fig. 1).

Some delay in filling of both lymph nodes and vessels was noted in those animals in which non selective injection of Thorotrast into the peritoneum had



Fig 2 Scintigram of the thorax and the upper part of abdomen following selective sub-diaphragmatic injection of $400 \text{ } ^{45}\text{Ca}^{45}\text{Tc}$ 5) 4 000 channel collimator 5—15 minutes after injection. The right and left group of lymph nodes in the upper anterior mediastinum cannot easily be separated b) Pinhole collimator 20—25 minutes after injection. The two groups of lymph nodes are easily separated.

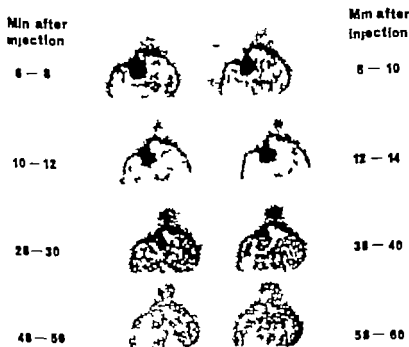


Fig 3 Scintigram of the thorax following injection of $400 \text{ } ^{45}\text{Ca}^{45}\text{Tc}$ 5) 4 000 channel collimator delayed (cf Fig 2)

not mix non selective intraperitoneal injection. The filling of the lymph nodes

Table 3
Results after intraperitoneal Tc^{99m} S colloid

		N of animals	Time of first filling of the lymph nodes
Non selective	No drug	3	12-20 minutes
	Hyalase	3	15 minutes general circulation
	PPP	2	4-6 minutes
Selective	No drug	3	4-8 minutes
	Hyalase	2	4-10 minutes
	PPP	2	3-4 minutes

been performed (Table 2). Hyaluronidase seemed to enhance the rate of uptake of the medium following both selective and non selective injections. When polyphloreton phosphate was used, the lymph nodes appeared after one hour but filling of the lymph vessels was not apparent until 24 hours. The contrast concentration within the lymph nodes was decreased compared to that in those animals examined without polyphloreton phosphate.

In no animal in group I were vessels other than those in the parasternal regions demonstrated. The results for injection of Tc^{99m} S colloid appear in Table 3. Following selective subdiaphragmatic injection of the radioactive colloid the upper anterior mediastinal lymph nodes were filled after 4 to 6 minutes (Fig. 2); the demonstration of the same nodes after non selective injection required however 12 to 20 minutes (Fig. 3). The uptake of the radioactive colloid gradually increased in these lymph nodes over 2 to 5 hours after which a balanced state was reached (Fig. 4). Following prior non selective injection of hyaluronidase, the resorption in the lymph vessels was unchanged. In one animal the lymph nodes were revealed at 15 minutes and in 2 animals a general filling of the thorax and head was apparent on the screen, indicating direct uptake of radionuclide in the systemic circulation. After polyphloreton phosphate the uptake in the lymph nodes was early, but the concentration within the nodes was less than in animals in which no polyphloreton phosphate had been used. In no instance was a lymphatic vessel directly evident on the scan. When the injection of Tc^{99m} S colloid occurred subsequent to intraperitoneal Thorotrast the upper anterior mediastinal lymph nodes failed to be demonstrated with the gamma camera. However an increase in radioactivity was observed at the site of these nodes and vessels indicating that there was no complete lymphatic blockage. Following the previous intraperitoneal Tc^{99m} S colloid however normal demonstration of the lymph nodes with Thorotrast was possible.

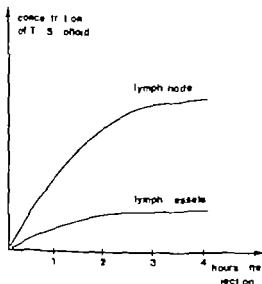


Fig 4 Concentration of $^{99}\text{Tc}-\text{S}$ colloid in the lymph nodes in the upper anterior mediastinum and parasternal lymphatics evaluated from the cine scintigram following intraperitoneal injection of 400 μCi $^{99}\text{Tc}-\text{S}$ colloid. Successful accumulation of the colloid in the lymph nodes and in the lymphatics. A balanced state is obtained in the lymphatics after 2 hours and in the lymph nodes after 3.5 hours.

Discussion

Knowledge of the condition of parasternal and anterior mediastinal lymph nodes prior to planning of radiation therapy or surgical treatment of a neoplasm within the region of its drainage is obviously desirable. The most common growth to which such a consideration should apply is carcinoma of the breast. It has been stated (ROUVIERE 1932; TURNER WARWICK 1958) that 75 per cent of the lymph flow from the breast is to the axillary nodes whilst 25 per cent is to the parasternal lymphatic trunks. ANDREASSEN *et al.* (1954) reported that a third of all carcinomas in the medial part of the breast metastasized to the parasternal lymph nodes compared to a tenth of those in the lateral part of the breast. The importance of knowing the condition of such nodes in each patient is therefore obvious.

The injection of Thorotrast into the peritoneal cavity is commonly used experimentally to demonstrate the parasternal and mediastinal lymph vessels (BARER 1961; BROVELLI *et al.* 1936; ESKIND 1940; HELD 1932; MENVILLE *et al.* 1932; OLIN *et al.* 1964; POWERAN 1934). Non selective injection in the lower part of the abdomen is followed by rapid dispersal of the contrast medium throughout the peritoneal cavity due to intestinal peristalsis. The medium thus comes into contact with the subdiaphragmatic lymphatics relatively soon and is absorbed. However, selective injection under the diaphragm ensures a more rapid uptake of the medium and both lymph nodes and vessels are demonstrated sooner than after non selective injection. Earlier filling of the

lymph nodes than of the lymph vessels may be explained by blockage of sinusoids in the glands followed by stasis within the afferent lymphatic trunks as resorption continues. It should be noted that the long half life of radioactive Thorotrast and its retention by the reticuloendothelial system precludes its use in man.

The use of $^{99}\text{Tc}^m$ S colloid and imaging by a gamma camera provided in the present research an experimental model which might be applicable to man. The filling of lymph nodes was more rapid than with Thorotrast and uptake was enhanced by selective subdiaphragmatic injection. Unfortunately the individual lymph trunks could not be demonstrated by this method due to the poorer resolution of the scintigram as compared to the roentgenogram. However this disadvantage is offset by the absence of side effects following the intraperitoneal administration of $^{99}\text{Tc}^m$ S colloid and the absence of peritonitis or other abnormality within the peritoneal cavity at autopsy. Our experience is in agreement with previous descriptions of the use of $^{99}\text{Tc}^m$ S colloid in man (ATKINS et coll 1970) and providing the position of the catheter be carefully controlled by fluoroscopy to avoid injection into the abdominal or intestinal wall, this method is particularly safe.

With Thorotrast as contrast medium, it was possible to increase the resorption from the peritoneal cavity after injection of hyaluronidase when the non selective technique had been employed. When $^{99}\text{Tc}^m$ S colloid was used hyaluronidase had no effect on the scintigram of the lymph nodes either in selective or non selective examinations. With the latter the resorption into the systemic circulation was enhanced and a diffuse filling of the whole animal appeared on the screen but no distinct lymph nodes were visible.

Polyphloreton phosphate has an anti hyaluronidase effect and decreases resorption from the peritoneal cavity (FRIES 1956). In the rabbits examined, filling of lymph nodes with both Thorotrast and $^{99}\text{Tc}^m$ S colloid occurred at the normal time following polyphloreton phosphate injection. However the concentration of the contrast media in the lymph nodes was less than in animals in which no polyphloreton phosphate was given.

One reason for differences between the present results and those of FRIES (1956) is that he used a dose three times larger. In addition he injected polyphloreton phosphate about 2 hours before the beginning of the resorption examination.

Other methods of examining lymph nodes regional to the breast include direct lymphography (KERR et coll 1970) in which patent blue is injected in the areolar region followed by cannulation of a lymph trunk and injection of a contrast material. Such an examination is technically difficult to perform and has the disadvantage that the lymphatic structures disclosed may not be regional

to the tumour and thus of doubtful relevance to the disease process. Radiogold (^{198}Au colloid) has also been used to scan the parasternal space, the isotope being injected subcutaneously on both sides of the xiphoid process of the sternum (DITTHELM 1966, ROSSI & FERRI 1966, SCHENK 1966). Such examinations have resulted in poor resolution and somewhat irregular filling of lymphatic structures. In addition, the locally absorbed radiation dose from ^{198}Au may be high (HAUSER *et al.* 1969) and radiation necrosis has ensued. This is in marked contrast to $^{99}\text{Tc}^m\text{S}$ colloid which gives a considerably lower locally absorbed dose with a physical half life of only six hours.

In summary these experiments describe a method of demonstrating parasternal lymph vessels and upper anterior mediastinal lymph nodes by a method that may offer considerable advantages when applied in man. The dynamic aspects of the scanning technique with a gamma camera may also prove of significant importance.

SUMMARY

Two groups of rabbits were examined. Thorotrast being injected into the peritoneal cavity in group I and $^{99}\text{Tc}^m\text{S}$ colloid used as the contrast medium in group II. The usefulness of the techniques is discussed and other methods and contrast media compared.

ZUSAMMENFASSUNG

Es wurden zwei Gruppen von Kaninchen untersucht. Der 1. Gruppe wurde Thorotrast in den Peritonealraum der 2. Gruppe $^{99}\text{Tc}^m\text{S}$ Kolloid als Kontrastmittel injiziert. Der Brauch beider der Technik wird diskutiert und andere Methoden und Kontrastmittel werden verglichen.

RÉSUMÉ

Deux groupes de lapins ont été examinés par injection dans la cavité péritonéale de Thorotrast dans le groupe I et de colloid de $^{99}\text{Tc}^m\text{S}$ utilisé comme moyen de contraste dans le groupe II. Les auteurs examinent l'utilité de ces techniques et les comparent avec d'autres méthodes et d'autres moyens de contraste.

REFERENCES

- ANDERSSON M. E., DAHL I. and SÖRENSEN B. Glandular metastases in carcinoma of the breast. Results of operation. *Lancet* 266 (1954) 176.
 ATKINS H. L., HALPERN W. and PETERSON P. Visualization of mediastinal lymph nodes after intraperitoneal administration of $^{99}\text{Tc}^m\text{S}$ colloid. *Nachr. Med. (Stuttgart)* 9 (1970) 275.
 BAKER G. R. Studio radiografica della cavità peritoneale (In Italian). *Minerva chir.* 16 (1961).

- BROVELLI M. e DOLFINI G. E. La linfografia. (In Italian.) Radiol. med. (Torino) 23 (1936) 294.
- DIERHELM L. Elargissement due diagnostic de carcinome mammaire avec l'aide des isotopes. Sympos. Europ. Radiol. mammaire. Strasbourg 1-3 July 1966.
- ERIKSSON L. Experimentelle Untersuchungen über die Biologie des Peritoneums. Dissertation, Oslo 1940.
- FRIJS B. Polyphloretin phosphate—a hyaluronidase inhibitor—and hyaluronidase in prevention of intraperitoneal adhesions. Acta chir. scand. (1956) Suppl. No. 217.
- HAUSER W., ATKINS H. L. and RICHARDS P. Lymph node scanning with ^{99m}Tc sulfur colloid. Radiology 92 (1969) 1369.
- HELD A. Die Resorption von kolloidalen Thorium (Thorotrast) aus der Bauchhöhle. Z. ges. exp. Med. 80 (1932) 819.
- KETT N., VARGA G. and LUKACS L. Direct lymphography of the breast. Lymphology 1 (1970) 3.
- MENVILLE L. J. and AKE J. N. A roentgen ray study in absorption of Thorium dioxide from peritoneal cavity of albino rat. Proc. Soc. exp. Biol. (N.Y.) 30 (1932) 28.
- OLIN T. and SALDREIN T. The lymphatic pathway from the peritoneal cavity: a lymphangiographic study in the rat. Cancer Res. 24 (1964) 1700.
- PERSSON B. and NAVERTEN Y. Technetium 99m sulfide colloid preparation for scintigraphy of the reticuloendothelial system. Acta radiol. Ther. Phys. Biol. 9 (1970) 567.
- PONDERANZ R. Animal experiments with colloid Thorium: a study in lymphatic absorption. Radiology 23 (1934) 51.
- ROSSI R. and FERRI O. La visualizzazione della catena mammaria interna con ^{99m}Tc . Presentazione di una nuova methodica: la linfoscintigrafia. (In Italian.) Minerva med. 57 (1966) 1151.
- ROUVIERE H. Anatomie des lymphatiques de l'homme. Masson & Cie. Paris 1937.
- SALDREIN T. Experimental studies on spread of Rous sarcoma in rats. Acta path. microbiol. scand. (1963) Suppl. No. 162.
- SCHENK P. Sintiographische Darstellung des parasternalen Lymphsystems. Strahlentherapie 130 (1966) 504.
- TURNER WARWICK R. T. The lymphatics of the breast. Brit. J. Surg. 46 (1958) 74.

PERCUTANEOUS REMOVAL OF INTRAVASCULAR FOREIGN BODIES BY THE SNARE TECHNIQUE

I ENGE and A FLATMARK

Retained intravascular foreign bodies entail a high risk of septicemia perforation aneurysm or thrombus formation and should usually be promptly removed. This may be done either by direct surgical intervention or by the so-called percutaneous transluminal snare technique (CURRY 1969 1970 DOTTER et coll 1971 McSWANEY & SCHWARTZ 1971 MILLER 1971 MAXWELL & ANDERSON 1972 RANDALL 1972). When located within the heart and central vessels foreign bodies should preferably be removed by the latter method thus avoiding thoracotomy. The principle of the snare technique and its employment in 3 patients are described.

Method. The left side of the heart and almost any part of the arteries in the chest may be reached by catheterization from the femoral artery. The right side of the heart the pulmonary arteries and the great systemic veins are conveniently available by catheterization from the femoral vein. If not visible in conventional film the foreign body may be localised by angiography (cf. Case 1).

After percutaneous introduction of a suitable catheter a double guide wire is passed through its lumen and slightly beyond its tip. A loop can now be formed by drawing one end of the guide wire and pushing the other (Fig. 1) the

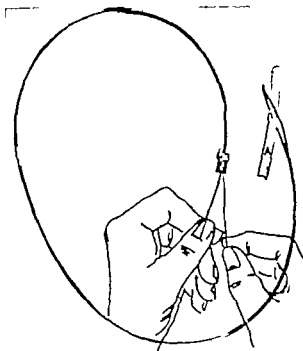


Fig. 1 Case 1 The principle in the formation of loop A. The teflon tubing removed.

loop together with the catheter is then manoeuvred under fluoroscopic control towards the foreign body which is snared. If not too large the foreign body may then be removed via the percutaneous route otherwise it is lodged in a peripheral vessel and dealt with by minor surgical intervention.

Case reports

Case 1 Female aged 48 with a subclavian steal syndrome due to a short occlusion of the right subclavian artery. A free flow in the right common carotid artery was secured by an internal shunt during an operation. A teflon tube of appropriate size (8 cm long OD 8 mm) had been introduced through a small carotid artery incision but during the manipulation the tube was suddenly caught by the blood stream and disappeared. Following insertion of a second shunt the subclavian artery was repaired by thrombolytic resection and vein patch graft from the saphenous vein. This tube was removed and the incision closed. Normal pulsation in the right common carotid and radial arteries was present at the end of the operation. Clinically it was impossible to diagnose the site of the lost tube. There was normal pulsation in the left carotid, subclavian and both femoral arteries. The patient still under general anaesthesia was brought to the roentgen department but the tube could be localised neither by fluoroscopy nor conventional roentgenography. Thoracic aortography performed by catheterization from the right femoral artery disclosed that the tube was lodged in the left subclavian artery and this was further confirmed by subsequent selective angiography (Fig. 1). The angiography catheter was



Fig. Angiography of the left subclavian artery. The lumen of the internal shunt (→) retrogradely filled with contrast medium. The lower end of this tube (↔) extends into the lumen of the aortic arch. A: Catheter. B: Internal mammary artery.

then replaced by 65 cm of teflon tubing (OD 3.0 mm ID 2.0 mm) and double guide wire (Cook teflon coated PE 160) passed through its lumen under fluoroscopic control. After several attempts the invisible teflon tube was successfully snared and guided down to the distal part of the abdominal aorta and released (Figs 3-4). Repeat angiography revealed the tube in the left common iliac artery from where it was subsequently removed in a small abdominal incision. The patient emerged under anaesthesia for total of 10 hours. She had an uneventful recovery and more than 1 year later still has normal pulsation in the right common carotid and radial arteries and no steal symptoms.

Case 2: Female aged 78 with an intracardiac pacemaker implanted one year previously for S.A. blockage had six months later had recurrent episodes of septicaemia. Removal of the pacemaker was planned. The previous pacemaker thread with its electrode could however not be removed even though it was directly pulled on at operation. Subsequently the patient had several episodes of dangerous septicaemia probably caused by the retained electrode from the pacemaker and as a result referred for an attempt at its removal by the SCI Lehman catheter No. 10 was cut obliquely to 1 cm and inserted into the right femoral vein. A 145 cm teflon catheter was inserted and with a second bend 2 cm from its end as a snare. Under fluoroscopic control of the pacemaker thread (Fig. 5) the inner half of the right tibia and entire radius. She has been symptom free for 10 months.

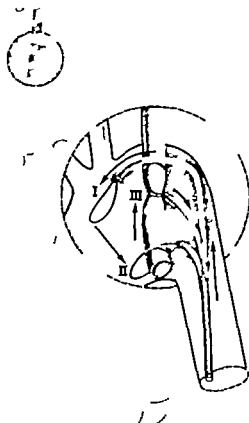


Fig 3 The stepwise procedure on snaring the lost teflon tube. The loop is formed (I), passed over the tube (II) and eventually snares it (III).

Table
Locations and type of retrieved foreign body in 52 cases

Location		Type	
Right atrium	14	Polythene tubing	20
Right ventricle	5	Guide wire fragments	3
Pulmonary artery	3	Cardiac catheter fragments	2
Subclavian artery	5	Pacemaker catheter fragments	4
Inferior vena cava	2	Holter al (distal segment)	
Iliac vein	1	Teflon tubing (internal shunt)	1
Descending aorta	2		

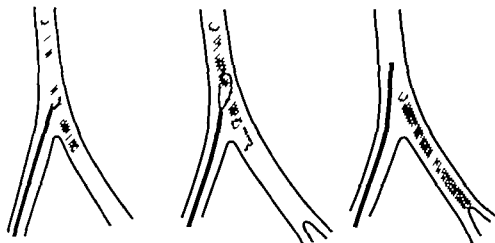


Fig 4 The teflon tube in the distal aorta with its stepwise release and lodging in the left common iliac artery

Case 3 Female aged 61 with an intracardiac pacemaker implanted in 1968 for complete AV blockage that has ever had to be changed four times over the next 4 years due to insufficient triggering. Two pacemaker threads with electrodes were cut and left in situ; one of these disappeared but was located in the right iliac vein. By the snare technique the pacemaker thread was promptly removed in the percutaneous route without any discomfort to the patient nor any late complications.

Comments

The present cases prove that percutaneous catheterization combined with the so-called snare technique is a safe and fast method for removing intravascular and intracardiac foreign bodies. The alternative treatment in Case 1 included open thoracotomy and possible arteriotomy of the aorta. The shunt could be removed by a small laparotomy incision and arteriotomy of the common iliac artery to avoid a long and more complicated surgical procedure. In the second case direct surgical attempts to remove the pacemaker thread had been unsuccessful, but it could easily be snared and dealt with percutaneously. Several past reports have indicated the usefulness of this snare technique with foreign bodies located in the right side of the heart or central systemic veins such as broken off pieces of catheter tubing or guide wires (Table). It would appear that this convenient and simple procedure should always be tried before direct surgical approach is undertaken.

Although special devices for the percutaneous transluminal removal of intravascular foreign bodies are available (Coxon 1969 1970) the snare technique

is more simple. As demonstrated in the present cases it may when needed readily be improvised. The second bend a short distance from the end of the snare is an important detail for it facilitates the catching and snaring of the foreign body by encompassing the entire lumen of the vessel.

SUMMARY

The principle of the percutaneous transluminal snare technique is described. The procedure enabled foreign bodies successfully to be removed in three patients.

ZUSAMMENFASSUNG

Das Prinzip der perkutanen transluminalen Schlingentechnik wird beschrieben. Das Verfahren ermöglichte die erfolgreiche Entfernung fremder Körper bei drei Patienten.

RÉSUMÉ

Description du principe d'un cerclage coulant intravasculaire introduit par une ponction percutanée. Cette technique a permis de retirer des corps étrangers intravasculaires chez trois patients.

REFERENCES

- CURRY J. L. Recovery of detached intravascular catheter or guide wire fragments. *Amer J Roentgenol* 105 (1969) 894.
- Recovery of detached catheter fragments. *J Amer med Ass* 211 (1970) 156.
- DOTTER C. T., ROSCH J. and BURROU M. K. Transluminal extraction of catheter guide fragments from the heart and great vessels: 29 collected cases. *Amer J Roentgenol* 111 (1971) 467.
- MAXWELL D. D. and ANDERSON R. E. Transfemoral retrieval of an intracardiac catheter fragment using a simple hook-shaped catheter. *Radiology* 103 (1972) 213.
- MCSANEY W. J. and SCHWARTZ D. C. Retrieval of a catheter foreign body from the right heart using a guide wire deflector system. *Radiology* 100 (1971) 61.
- MILLER R. E. Removal of a foreign body from the lung by angiographic snare technique. *J thorac cardiovasc Surg* 61 (1971) 624.
- RANDALL P. A. Percutaneous removal of iatrogenic intracardiac foreign body. *Radiology* 107 (1972) 591.

CONGENITAL VASCULAR MALFORMATIONS OF THE HAND

U ERIKSSON and A HEMMINGSSON

Arteriovenous vascular malformations occur in most organs in which arteries and veins run parallel (STEINBERG et coll 1963) their names vary e.g. haemangioma simplex cavernous haemangioma congenital arteriovenous fistula or aneurysm, etc (SZILAGYI et coll 1965) Angiographically demonstrated vascular malformations of the hand have been reported by CROSS et coll (1958) in 2 cases and SZILAGYI et coll (1965) in 4 cases

These vascular malformations probably have their origin in an anomalous development of the embryonic vascular system (REINHOF 1924 REID 1925 DE TARANT 1932 SZILAGYI et coll 1965) Different forms of primitive communications between the arterial and venous systems thus conceivably may persist, depending upon the stage at which the anomalous development occurs. Four illustrative cases of arteriovenous malformations of the hand are now described

Method Angiography was performed with a thin walled (J. Odman catheter) introduced into the ulnar artery through which 10 ml of contrast medium (Angiografin) were injected with a Casali pressure syringe at 3 kP/cm at a pulse frequency of 1

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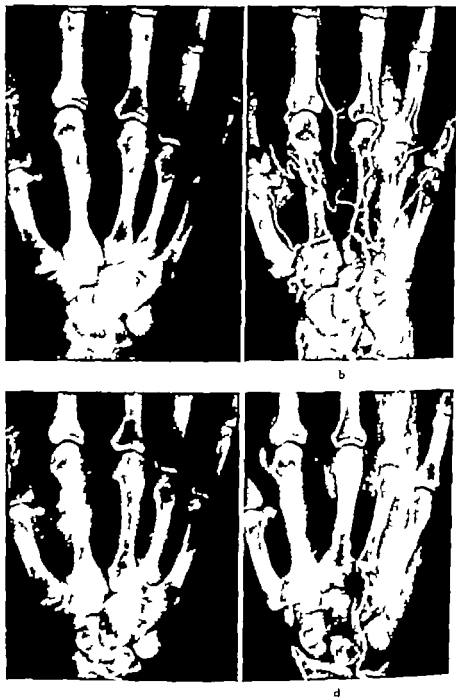


FIG. 1. Case 1. a) Conventional radiography of the hand. b) Arterial and c) venous phase after intraarterially administered bradykinin. d) Same phase (b) without bradykinin.

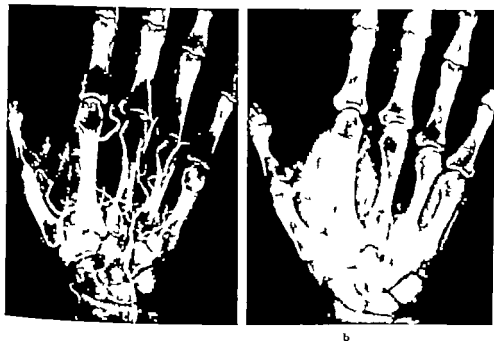


Fig. Case 2. Angiography: a) Arterial and b) venous phase.

franc/s. Bradykmin was injected intraarterially through the catheter at a dose rate of about 10 $\mu\text{g}/\text{min}$ during 10 minutes immediately before the injection of the contrast medium (ERIKSSON 1969, 1970).

Case reports

Case 1. Female, aged 51 with swelling on the dorso-radial aspect of the right hand from childhood was operated upon in 1976 and 1960 and haemangioma extirpated followed by almost immediate recurrence.

Cystic lesions with thickening of the cortex of the second and third metacarpals as well as an increase in length of these bones were observed (Fig. 1 a). Angiography following the intraarterial administration of bradykmin revealed a vascular malformation with contrast filling of round, irregular cavities about the size of the head of a pin in which the contrast medium remained for several seconds (Fig. 1 b). No early venous filling occurred. Bradykmin improved the definition of the peripheral arteries which also filled more rapidly (Fig. 1 b, d). The anomalous veins were not affected.

Operation was performed in 1980 with excision of the vascular mass. Histology revealed fibrous connective tissue containing endothelium coated partly blood filled cavities and in some areas med by granulation tissue. The appearances are compatible with cavernous haemangioma.

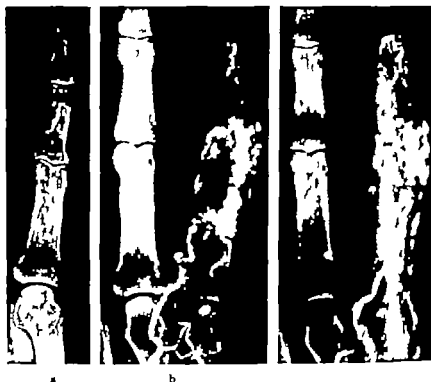


Fig. 3. Case 3. a) Conventional radiography of digit 5. Angiography. b) Arterial and c) venous phase.

Case 2. Female, aged 47, who since birth had had a bluish swelling on the palmar aspect of the right wrist in the region of the thenar eminence and one on the palmar aspect of the distal phalanx of the right thumb.

Operation was carried out in 1945. A fascicular tumour was extirpated but early recurrence occurred. No further operative measures were performed. The bones of the hand were normal. Angiography revealed vascular changes as in Case 1, with filling of round cavities in which the contrast medium remained for several seconds (Fig. 2). No early venous filling as observed. Bradykinin had the same effect as in Case 1.

Case 3. Male, aged 49, who had had a bluish, slightly compressible tumour on the right little finger since he was 15 years of age. Cystic lesions in the proximal and second phalanges were present (Fig. 3 a). Angiography revealed anomalous communications between the arterial and venous system with irregular tortuous wide fistulas and early venous filling (Fig. 3 b, c). Bradykinin produced the same effect as in the previous cases. Operation consisted of amputation through the middle of the proximal phalanx. There was no recurrence.

Case 4. Female, aged 54, who had had more rapid growth of her left hand from the age of 3 years. The skin of the hand had become thin and slightly ulcerated in recent years.

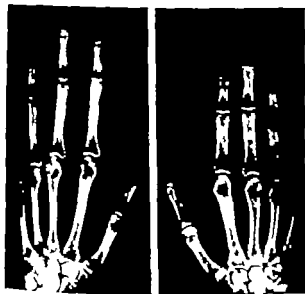


Fig. 4 Case 4 Conventional radiograph of the hands

The left forearm was 3 cm longer than the right and digits 2, 3 and 4 on the left side were 2 to 3 cm longer than the corresponding digits on the right side. Cystic alterations, thickening of the cortex and lengthening of the proximal and second phalanges of digits 2 to 5 as well as lengthening of the metacarpal bones of the same digits were observed (Fig. 4). Preoperative angiography disclosed vascular malformation with contrast filled cavities and in addition wide tortuous fistular communications between the arterial and venous system with early venous filling (Fig. 5 a, b). The malformed vessels were apparently supplied exclusively from the ulnar artery.

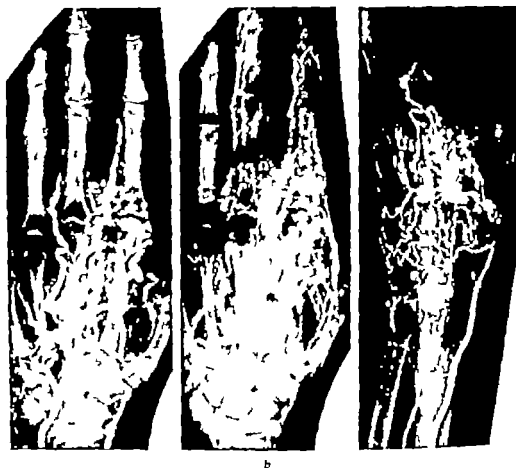
Operation consisted of excision of the ulnar artery distal to the origin of the interosseous artery and of the branch of the ulnar artery supplying digit 2. Numerous small thin walled cysts were also removed. Necrosis of the skin occurred postoperatively necessitating amputation of digits 2 and 3 through the metacarpal bone and plastic surgery with split graft and skin flap.

Angiography 1½ years later disclosed recurrence of the vascular malformation. The malformed vessels were receiving their blood supply from the dilated radial artery arising from the ulnar artery (Fig. 5 c).

No other malformation were evident in any of the patients.

Discussion

WOOLLARD (1972) distinguished three stages in the development of the vascular system: the capillary stage with intercommunication between the arterial and venous parts; the retiform stage with narrow channels that tend to be confluent with both parts; micro- and macrovascular stage with development of a grossly mature vascular system but with anomalous



b

Fig. 5 Case 4. Angiography: a) Arterial and b) venous phase before operation; c) Arterial phase after operation.

components. Cases 1 and 2 of the present report may be assigned to the capillary stage with its primitive blood filled cavities or lacunae, between the arterial and venous systems and Cases 3 and 4 to the retiform stage with fistular communications between the arterial and venous sections. The anomalous immature vessels were not affected by bradykinin, possibly due to the absence of a muscular layer (cf. ERICSSON 1970). The considerably improved circulation to the hand after the bradykinin injection facilitated assessment of the extent of the alterations.

Cystic skeletal lesions in the phalanges were present in 3 of the patients. This is an important sign of interosseous vascular malformation (KOLAR *et al.* 1966). If the malformation is of the macro-fistular type, with its greatly increased blood flow, conservative surgery will give rise to a recurrence so that

amputation of the affected bone must be carried out (Cross et coll 1958). Both conventional radiography and angiography are thus of value in determining the extent of the alterations in soft tissues and bone. Case 4 in which excision of the vascular mass only in the soft tissues and of the main afferent artery (ulnar artery) led to the opening up of new afferent arterial main branches (radial and intraosseous arteries) is an example. The paradoxical occurrence of ischaemic ulceration combined with increased vascularization that characterizes these vascular malformations (Cross et coll 1958) was also apparent. The lengthening of the bones in this patient and in one of the others indicates that the increased blood flow was already present before the closure of the epiphyses (Dr TAKATS 1932).

The Bradykinin was kindly supplied by Sandoz, Basel.

SUMMARY

Different types of vascular malformations of the hand are described and related to the embryonic development. The importance of preoperative determination of the interosseous extent and the angiographic appearances of the changes is pointed out. Bradykinin facilitates this determination by improving the peripheral circulation.

ZUSAMMENFASSUNG

Verschiedene Typen von vaskulären Missbildungen der Hand werden beschrieben und der embryonalen Entwicklung zugeordnet. Die Bedeutung der präoperativen Bestimmung des interknochernen Ausmaßes und des angiographischen Bildes der Veränderungen wird hervorgehoben. Bradykinin erleichtert diese Untersuchung durch Verbesserung der peripheren Zirkulation.

RÉSUMÉ

Les auteurs décrivent différents types de malformation vasculaire de la main et les rapprochent du développement embryologique. Ils soulignent l'importance de la détermination préopératoire de l'extension inter-osseuse et insistent sur l'aspect angiographique des lésions. La bradykinine facilite cette détermination en améliorant la circulation périphérique.

REFERENCES

- CROSS F. S., GLOVER D. M., SODERBY F. A. and OLDFIELD G. A. Congenital arteriovenous aneurysms. *Ann Surg.* 148 (1958) 649.
Dr TAKATS G. Vascular anomalies of the extremities. *Surg. Gynec. Obstet.* 55 (1932) 227.
EKTOROV U. Effect of bradykinin, acetylcholine and histamine upon the blood flow of the amputation stump of leg amputees. *Scand. J. Clin. Lab. Invest.* 24 (1969) 129.

- Effect of local intraarterial administration of bradykinin and hydrgenic m obstructive arterial disease. *Acta radiol. Diagnosis* 10 (1970) 449
- KOLAR J, BEK V, VRABEC R und SCHWANE R. Röntgenologische Nativbefunde bei Gefäßmissbildungen der Haut und der Unterhautgewebe. *Fortschr. Röntgenstr.* 105 (1966) 245
- REID M R. Studies on abnormal arteriovenous communications acquired and congenital. I. Report of a series of cases. *Arch. Surg.* 10 (1952) 601
- REINHOFF W F. Congenital arteriovenous fistula. An embryological study with the report of a case. *Johns Hopk. Hosp. Bull.* 33 (1924) 271
- SZILAGYI D E, ELLIOTT J P, DeRUSSO F J and SMITH R F. Peripheral congenital arteriovenous fistulas. *Surgery* 57 (1965) 61
- STEINBERG I, TILLOTSON P M and HALPERN M. Roentgenography of systemic (congenital and traumatic) arteriovenous fistulas. *Amer. J. Roentgenol.* 89 (1963) 543
- WOOLLARD H H. The development of the principal arterial stems in the forelimb of the pig. *Cont. Embryol. Carneg. Instr.* 14 (1922) 139

ROENTGEN AREA PRODUCT AND EXPOSURE MEASUREMENTS DURING CHEST RADIOGRAPHY AND NEPHROTOMOGRAPHY

S C BUSHONG M J POGONOWSKA, A J GERLOCK S A GLAZE and
D G GLAZE

There is increasing concern over patient exposure during diagnostic radiographic procedures and this concern has been expressed by radiation scientists in refereed journals (MORGAN 1969 McCLELLAHAN 1970 SAGAN 1971) as well as by non scientists in the lay press (NADER 1968). This concern has been generated because of reports (GITLIN & LAWRENCE 1966 BROWN et al 1969) of increasing radiation utilization in medical and dental diagnosis and because of possible latent deleterious effects of this increase in exposure. Estimates of patient gonadal dose and of dose to other organs during various diagnostic examinations have been made for a number of years. These estimates however have usually relied on measurements with ionization chambers and more recently on measurements with thermoluminescent dosimeters.

Instrumentation is now available in the form of a transmission type ionization chamber which can be retrofitted to any diagnostic machine and which measures the roentgen area product (R cm²) during any type of examination. The details of this instrumentation have been described thoroughly (MORGAN & GERRET 1966 ARNOLD & CROOKS 1965 PYCHLAU 1967) and will not be reviewed here.

Table I

Simultaneous roentgen area product and exposure measurements during chest examination

Exposure	N. of patients	Average R cm	Average R
Posterior-anterior projection			
64/10	6	11.92	0.070
72/10	19	19.44	0.039
74/10	49	23.86	0.036
78/10	12	21.10	0.075
82/10	18	27.63	0.081
84/10	18	35.86	0.080
90/20	11	61.09	0.093
Lateral projection			
104/15	39	52.94	0.089
110/20	12	9.15	0.160
110/30	21	143.18	0.207
110/4	17	246.64	0.317
120/1	12	68.10	0.081

The purpose of this paper is to report measurements for two selected types of diagnostic examination which show that under clinical conditions, the R cm measurement being linearly related to the exposure to the local tissue in the primary beam can be conveniently used to estimate patient exposure.

Methods and Materials We have employed a Diamontor (Nuclear Associates Inc.) as our R-cm meter for obtaining this data for chest radiography and nephrotomography. Before each examination one packet of three lithium fluoride (LiF) high sensitivity ribbons (TLD 100 Harshaw Chemical Co.) was taped to the skin of the patient in the center of the radiation field. During the chest examinations, the dosimeters were left for several successive examinations while during nephrotomography one set of dosimeters was used for each patient. Dosimeters were also taped to both sides of a 0.5 mm Pb protective apron at gonadal level for several successive examinations. The dosimeters were enclosed in 1.3 cm diameter 0.005 cm thick polythion tubing (Polyplastic Products, Inc.) and each package of dosimeters was precisely identified for radiation sensitivity with a batching calibration factor. Analysis of the clinically employed dosimeters was based on a comparison with the thermoluminescence of control dosimeters receiving a known quantity and quality of exposure. All of the results for the chest examinations were obtained with the same roentgen machine in the chest clinic of the Ben Taub General Hospital. The unit had the following emission

Table 2

Simultaneous roentgen area product and exposure measurements during nephrotomography

kVp mAs	N of films	N of tomograms	R cm	R
78/130	1	8	1388	4.946
68/750	2	6	1407	1.860
72/760	2	8	1548	.72
68/270	2	6	2085	4.877
74/760	2	8	2180	2.980
760	1	9	2647	5.807
67/760	4	7	1585	4.74
74/380	2	8	297	3.883
72/370	2	8	3418	3.997
76/360		8	3554	5.809
4/60	3	8	3586	12.490
80/360		8	3840	7.064
78/360	3	8	4007	10.810
78/360	2	9	4144	7.176
87/370	3	8	4306	8.507
76/370	2	9	4324	5.912
74/540	2	8	4627	15.110
8/370	2	8	6060	17.740
78/360	2	9	6356	15.470

characteristics HVL = 3.8 mm Al at 80 kVp 126 mR/100 mAs at 183 cm FFD. The field size was fixed at 35.5 cm \times 43 cm at the film distance for all examinations. The tomographic results were all obtained with a Siemens Universal Planigraph. HVL = 3.1 mm Al at 80 kVp 205 mR/100 mAs at 140 cm FFD. All of the tomographic films were taken with a 25.5 cm \times 30.5 cm field size. The survey films were taken at 100 cm FFD with a field size of 35.5 cm \times 43 cm.

Results

Tables 1 and 2 show the data derived from analysis of the TLD and from the R cm meter for the chest examinations and the nephrotomograms respectively. Table 3 reports the results of measurement with TLD designed to show the effectiveness of gonadal shielding during the examinations. Under our clinical condition gonadal dose reduction factors of 1 and 2.33 were shown for the lateral chest and nephrotomogram respectively. All of these data resulted from examinations that were conducted at various conditions of kVp and mAs and even for various numbers of films. The field size for each type of examina-

Table 3

Gonadal exposures during chest examination and nephrotomography and effect of shielding

Exam	No. of patients	Shielded gonadal R	Unshielded gonadal R	Dose reduction factor
P	72	0.0018	0.0015	0
Lat	84	0.0025	0.0032	1.28
Neph	10	0.0308	0.0719	2.33

tion were constant. Usually the chest examination consisted of one p.a. and one lateral film. The operating conditions ranged from 64 kVp/10 mAs to 90 kVp/20 mAs for the p.a. film and from 104 kVp/15 mAs to 120 kVp/15 mAs for the lateral film. The 12 exposure conditions reported in Table 1 are the most frequently employed in our clinic.

The nephrotomogram usually consisted of one or two 35.5 cm \times 43 cm survey films of the abdomen, followed by six to eight 25.5 cm \times 30.5 cm tomographic films and the conditions of kVp and mAs varied considerably. Table 3 points out these differing conditions. In each procedure, the measurements reported from both the R-cm meter and the thermoluminescent dosimeters followed the total examination. Figs 1 and 2 are graphical representations of the data of Tables 1 and 2 and show that the relationship between the R-cm measurement and the local tissue exposure is linear for each diagnostic procedure regardless of the conditions of operation, i.e. kVp, mAs, and FFD.

Discussion

That the relationship between R-cm and exposure is linear is not surprising. There are five factors that significantly affect the output of an x-ray machine whether that output be measured in R or R-cm: (1) kVp, (2) mAs, (3) filtration, (4) distance and (5) field size. If the output of a machine is determined for a particular type of examination, then only (1) and (2) affect the magnitude of this output since (3), (4) and (5) are constant for that given type of examination. A variation in kVp/mAs would then be expected to result in proportionate changes in both R-cm and R.

Our findings substantiate this rationale and demonstrate that the R-cm meter is an accurate and convenient way to estimate patient exposure during diagnostic examinations. The slope of the linear relationship for p.a. and lateral chest examination was 503 R-cm/R and 701 R-cm/R respectively. This value

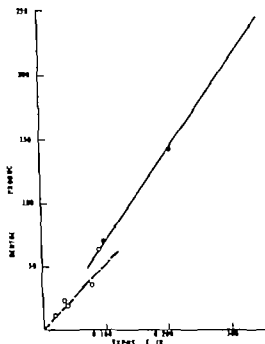


Fig. 1 The relationship between roentgen area product and exposure for chest radiography. The slopes of the line for p (---) and lateral (—) examination are 503 R-cm/R and 701 R-cm/R respectively.

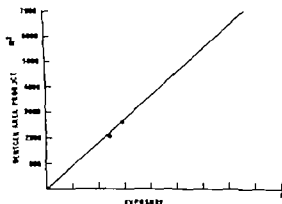


Fig. 2 The relationship between roentgen area product and exposure for nephrotomography. The slope of the line is 454 R-cm²/R.

for the nephrotomographic examinations was 454 R-cm/R. Use of these calibration factors would allow an estimation of the patient exposure from an R-cm measurement for each of these types of examinations. Presumably a similar calibration factor is obtainable for all routine procedures.

CAMERON (1971) has suggested that this type of instrumentation is not only useful for estimating patient exposure but perhaps even necessary for the control

of excessive exposure. The control would follow the awareness by technicians and physicians of a conveniently measured unit of patient dose. CAMERON has also suggested that the output of an R-cm meter be expressed in a new unit the rap where one rap = 100 R-cm. This investigation shows that perhaps a new unit is not necessary since by the use of a simple conversion factor the patient exposure can be estimated from the R-cm measurement.

Our findings of roentgen area product and patient exposure are in general agreement with those of the other investigators. Following p.a. and lateral chest radiography the entrance exposure based on 234 patients, ranged from 20 mR to 317 mR and the roentgen area product ranged from 12 to 247. ROGERS (1969) has reported the average skin dose during chest radiography to be 13 mrad p.a. and 26 mrad lateral and CARLSSON (1965) reports a skin dose of 60 mrad and a roentgen area product of 530. ARNAL & PYCHIAU (1962) report an average roentgen area product of 121 for chest radiography. Nephrotomograms have been reported (VILLAUME 1965) to deliver 1300 to 1900 R-cm. Our measurements based on 19 patients resulted in values ranging from approximately 1300 R-cm to 6400 R-cm. The associated exposure values ranged from 4.8 to 15.4 R. These data show how unreasonable it is to use handbook figures to estimate patient dose post facto since the actual patient dose can vary by an order of magnitude depending upon the conditions of kVp/mAs.

Although many factors of a radiographic examination affect the exposure of the patient to radiation, an estimate of that exposure can be made conveniently with an R-cm meter attached to the roentgen machine. This type of dosimeter has many advantages over classical methods of estimating patient dose. Our finding of a linear relationship between R-cm and R for a given diagnostic radiographic examination supports its use in a routine clinical setting.

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We would like to thank Mrs Barbara Bradley for conscientious and faithful work with this project.

SUMMARY

Roentgen area product (R-cm) and exposure (R) measurements are reported for two types of routine diagnostic examination: p.a. and lateral chest examinations and nephrotomography. Roentgen area product measurements were made with transmission type ionization chamber retrofitted to the light localizing collimator of the roentgen machine. Patient exposure was determined with LiF (TLD 100) thermoluminescent dosimeters placed on the entrance surface of the patient in the center of the radiation field. The resulting data

are based on 234 chest examinations and 19 nephrotomographies. The relationship between R-cm and R was linear and had slope coefficients of 503.701 and 454 for p.a. chest, lateral chest and nephrotomography respectively. Gonadal shielding resulted in at least 20 per cent dose reduction.

ZUSAMMENFASSUNG

Die Verfasser berichten über das Bestrahlungs-Flächenprodukt (R-cm) und Expositionen (R) Messungen für zwei Formen diagnostischer Routineuntersuchungen p.a. und laterale Thoraxuntersuchungen und Nephrotomographien. Bestrahlungs-Flächenprodukt Messungen wurden mit einem Transmissions-typ einer Ionisationskammer vorgenommen die am licht lokalisierenden Kollimator des Röntgenapparats angebracht war. Die Patientendosis wurde mit LiF (TLD 100) Thermolumineszenz Dosimetern bestimmt die auf der Eintrittsoberfläche des Patienten im Zentrum des Bestrahlungsfeldes lagen. Die resultierenden Daten stützen sich auf 234 Thoraxuntersuchungen und 19 Nephrotomographien. Die Beziehung zwischen R-cm und R war linear und hatte Neigungskoeffizienten von 503.701 und 454 für p.a. Thorax, laterale Thorax/Balder bzw. Nephrotomographien. Schutz der Gonaden führt zu einer Dosiserminderung von mindestens 20 Prozent.

RÉSUMÉ

Des mesures du produit roentgen surface (R-cm) et de la dose d'exposition (R) ont été faites pour deux types d'examen de routine: les examens de face et de profil du thorax et la nephrotomographie. Les mesures Roentgen surface ont été faites avec une chambre ionisation de type transmission adaptée au collimateur localisateur lumineux de l'appareil radiologique. La dose d'exposition du patient a été déterminée par des dosimètres thermo luminescents à LiF (TLD 100) placés à la surface d'entrée du patient au centre du champ d'irradiation. Les résultats sont basés sur 234 examens thoraciques et sur 19 nephrotomographies. La relation entre R-cm et R est linéaire et a un coefficient de pente de 503.701 et 454 pour les radiographies du thorax de face, de profil et la nephrotomographie respectivement. La protection des gonades donne une réduction d'au moins 25 pour cent de la dose.

REFERENCES

- ANDRAY G. M. and CROOKS H. E. The measurement of patient dose. *Brit. J. Radiol.* 38 (1965) 766.
- ARNOLD M. L. and PYCHIA H. Exposure of the patient during roentgen diagnostic examinations. *Ann. N.Y. Acad. Sci.* 11 (1961) 247.
- CAMERON J. R. A proposed unit for patient radiation exposure from diagnostic x-rays. *Health Phys.* 21 (1971) 8-9.
- CARLSON C. Integral absorbed doses in roentgen diagnostic procedures. *Acta radiol. Ther. Phys. Biol.* 3 (1964) 384.
- GILLES J. N. and L. J. P. S. Population exposure to x-rays. U.S. 1964 Public Health Service. N. 1-6.
- MCCLELLAN J. I. X-ray radiology. 96 453.
- MORGAN K. Z. I. Radiation Benefit Criteria. *Health Phys.* 17 (1969) 539.

- MORGAN R. H. and GIBBERT J. C. The radiant energy received by patients in diagnostic x ray practice *Amer J Roentgenol* 97 (1966) 793
- NADLER R. Wake up America x rays unsafe *Ladies Home Journal* 85 (1968) 126
- PECHLAU P. Dose assessment in diagnostic radiology *Brit J Radiol* 40 (1967) 559
- ROGERS R. T. Radiation dose to the skin in diagnostic radiography *Brit J Radiol* 42 (1969) 511
- SAGAN L. A. Medical uses of radiation *J Amer med Ass* 215 (1971) 1977
- U. S. Department of Health Education and Welfare. Population dose from x rays U. S. 1964. Public Health Service No. 2001 (1969) 82
- VILLAUME C. The evaluation of the total irradiation exposure of patients during medical x ray diagnostic procedures. *Agfa Gevaert x ray Bulletin* 2 (1965)

